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Archives of Neurology and Psychiatry

Vol. 10 AUGUST, 1923 No. 2

THE DIENCEPHALIC CENTERS CONTROLLING ASSOCIATED LOCOMOTOR MOVEMENTS

AN EXPERIMENTAL RESEARCH *

HUGO MELLA, M.D.

BOSTON

One of the striking signs appearing early in many cases of paralysis agitans is the loss of the normal automatic, associated movements. In walking the normal quadruped alternates the movements of the legs by associating the left fore with the right hind, and the right fore with the left hind limb; in normal man we see the identical coordination between arm and leg movements. If now, a typical case of paralysis agitans is observed, it is seen that the arms are carried with the trunk and do not swing in coordination with the contralateral leg. That this is not due to the rigidity of the arms is obvious because many cases presenting this sign are not rigid, merely having the tremor and mask-like features characteristic of this syndrome.

The literature on automatic associated movements is indefinite and largely clinical. The papers published by those who have studied the basal ganglions experimentally, merely mention the presence of alternate walking movements in their preparations when these are observed, but make no attempt at a definite localization.

In working on the genesis and inhibition of extensor rigidity, Stanley Cobb [1] observed that these movements were lost when a transection was made just cephalad to the red nucleus and the present work is, in a sense, a continuation of that series of experiments. Walshe,[2] in a review of the work of Magnus, reports that these movements were observed with the thalamus and midbrain intact, cortex and striatum having been removed. Wilson [3] destroyed parts of the pallidum and putamen with the electric needle and after the animals recovered from the shock of the operation found no disturbance of motility or posture.

* From the Department of Neuropathology, Harvard Medical School.

1. Cobb, Stanley, Bailey, A. A., and Holtz, P. R.: On the Genesis and Inhibition of Extensor Rigidity, Am. J. Physiol. **44**:239, 1917.

2. Walshe, F. M. R.: The Work of Magnus and His Collaborators on the Nervous Regulation of Posture and Its Bearing on Some Modern Neurological Problems, Med. Science **7**:109, 1922.

3. Wilson, S. A. K.: An Experimental Research Into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:427, 1914.

There is much clinical and pathologic evidence indicating that the phenomena of the parkinsonian syndrome is caused by lesions in the basal ganglions. Jelgersma [4] in 1909, was the first to report these pathologic changes; more recently, Hunt,[5] Vogt [6] and Bielschowsky [7] have demonstrated the presence of degenerative processes in the pallidum in cases of paralysis agitans. Tretiakoff,[8] however, places the lesions in the substantia nigra.

In view of these various observations it was thought that a series of ablation experiments on the basal ganglions might lead to a more definite localization of this function and thereby throw more light on the pathology, mechanism and physiology of the parkinsonian syndrome.

METHOD OF INVESTIGATION

Normal cats were used in all the experiments. They were etherized, the carotids were ligated and a tracheal cannula was inserted. The rubber tube of the ether bottle was then attached to the cannula and the animal was placed in the prone position. Next, a free exposure of the calvarium was made and, commencing with a trephine opening, all bone was removed from the glabella to the tentorium, the dura being opened along the edge of the exposure and reflected from the cerebrum toward the midline. Anesthesia was discontinued and an assistant compressed the vertebral arteries, while with a small curved spatula, the cortex was shelled off leaving the basal ganglions and midbrain intact. The cranial cavity was sponged out lightly with pledgets of cotton moistened in warm saline solution; the cavity was then lightly packed with these pledgets, and the pressure on the vertebral arteries was released. When bleeding had ceased the incision was closed with clamps. If these steps were not performed with speed the animals succumbed, or the shock was so great that the reflexes did not return during the period of survival. The animal was then placed on an electric warming pad, and, if anesthetization and operation were well timed, recovery occurred in about ten to fifteen minutes. Observations were then made of the reflex movements and further ablations carried out by opening the wound, removing the moist packing with great care, and then, proceeding as before.

4. Jelgersma: Die anatomischen Aenderungen bei Paralysis agitans und chronischer Chorea, Verhandl. d. Gesellsch. deutsch. Naturforsch. u. Aerzte zu Köln, Leipzig, 1909.

5. Hunt, J. R.: The Efferent Pallidal System of the Corpus Striatum, A Consideration of Its Functions and Symptomatology, J. Nerv. & Ment. Dis. **46**: 211, 1917.

6. Vogt, C., and A.: Zur Lehre von den Erkrankungen des Striärensystems, J. f. Psychiat. u. Neurol. **25**:633, 1920.

7. Bielschowsky, Max: Weitere Bemerkungen zur normalen und pathologischen Histologie des Striärensystems, J. f. Psychiat. u. Neurol. **27**:233, 1922.

8. Tretiakoff: Contribution à l'étude de l'anatomie pathologique du locus niger, Paris, Jouve et Cie, 1919.

BRIEF PROTOCOLS OF EXPERIMENTS

EXPERIMENT 1.—Cat N-20-8, Nov. 29, 1920.

3:40 p. m. Removal of hemispheres; first the right, then the left. (Specimen *A*.)

3:45 p. m. Slight spasticity of the extensors of the legs.

3:50 p. m. Electric pad placed over the cat.

4:00 p. m. Moving tail from side to side and tip of tail up and down.

4:08 p. m. Made right and left alternate "walking" movements with front, but not hind, legs.

4:09 p. m. Attempts to rise.

4:25 p. m. Alternate "walking" movements—right hind and left fore, and left hind and right fore—when stimulated by rolling from side to side.

4:35 p. m. Transection made 5 mm. anterior to tentorium. (Specimen *B*.)

4:45 p. m. Anal stimulation: wags tail—no walking movements. Rigidity.

4:52 p. m. Transection at tentorium. (Specimen *C*.)

4:55 p. m. Gradual rigidity (extensor in type). No "walking" movements.

4:57 p. m. Animal killed.

EXPERIMENT 2.—Cat N-20-12, Dec. 7, 1920.

3:50 p. m. Decorticated. Transection through the basal ganglions, back to the level of the optic chiasm. (Specimen *A*.)

3:56 p. m. Moderate rigidity of all legs; fore greater than hind. Good sneeze, fair pinna and corneal reflexes; arched back.

4:10 p. m. No "walking" movements, but less rigidity.

4:17 p. m. Takes sitting position and tries to jump. Makes excellent alternate walking movements with all four legs. Walks on floor when supported by nape of neck.

4:26 p. m. Transection 5 mm. anterior to tentorium. (Specimen *B*.)

4:55 p. m. Makes alternate movements with fore legs, but not with hind. Rigid enough to stand.

5:00 p. m. Transection at tentorium. (Specimen *C*.)

5:07 p. m. Very rigid; marked opisthotonus.

5:15 p. m. Animal killed.

EXPERIMENT 3.—Cat N-20-15.

3:20 p. m. Decortication and transection at the level of the optic chiasm. (Specimen *A*.)

3:40 p. m. Nictitating membrane, pinna and sneeze reflexes present.

4:00 p. m. "Walking" movements with fore legs.

4:10 p. m. "Walking" movements with fore and hind legs which alternate when the animal is placed on its abdomen with all legs spread out. The animal is able to crawl forward.

4:25 p. m. Same movements but better. Animal almost jumps from the floor.

4:40 p. m. Transection 4 mm. anterior to tentorium. (Specimen *B*.)
Some rigidity. No "walking" movements. Animal breathing badly.

5:01 p. m. Animal died.

EXPERIMENT 4.—Cat N-21-66, March 25, 1921.

11:18 a. m. Decorticated. (Specimen *A*.)
1 cm. of basal ganglions removed.

11:24 a. m. Slight spasticity. Excellent associated "walking" movements in fore and hind legs; also jumps.

11:42 a. m. Transection 4 mm. caudad to first transection. Respirations became rapid. (Specimen *B.*)

1:45 p. m. Very spastic. No "walking" movements. Attempts to raise its head; fore legs are flexed.

4:25 p. m. Transection at tentorium. (Specimen *C.*)

4:45 p. m. Very rigid in fore legs and neck, very little in hind legs and tail.

4:50 p. m. Died. Blood clot on base of skull extending from midbrain to level of eighth nerve.

EXPERIMENT 5.—Cat N-21-69, March 18, 1921.

3:17 p. m. Decorticated. Transection through anterior tip of basal ganglions. (Specimen *A.*)

3:25 p. m. Slight spasticity in fore legs; breathing quietly.

3:45 p. m. Corneal and pinna reflex absent. Considerable spasticity in all four legs.

3:50 p. m. Does not stand when placed on feet. Stimulating the tail results in no reaction.

4:06 p. m. No attempt at "walking" movements; wags tip of tail.

4:08 p. m. Alternate movements with hind legs but not fore legs.

4:17 p. m. Stimulating the feet results in alternating movements with hind legs and slight movements of left fore leg.

4:32 p. m. Stimulation of right ear: cat scratches right ear with right hind leg and flexes head to right.

4:45 p. m. Section at anterior colliculi. (Specimen *B.*)

4:50 p. m. No alternating "walking" movements. Immediate marked rigidity of fore legs, some of hind legs, tail erect. When animal is placed on its belly, stimulation of the feet causes flexion of legs; but no alternating movements are produced.

5:18 p. m. Died.

EXPERIMENT 6.—Cat N-21-89, April 12, 1921.

2:50 p. m. Decorticated. Basal ganglions intact. (Specimen *A.*)

3:00 p. m. Limbs spastic; sneeze, pinna and corneal reflexes present. Respiration very rapid.

3:07 p. m. Excellent alternating "walking" movements with all four legs. Makes galloping movements; waves tail. Breathes well.

3:15 p. m. Alternate fore and hind leg movements continue. Jumps from floor.

3:25 p. m. Section 2 mm. cephalad to tentorium. (Specimen B.)

3:33 p. m. Holds head up. No "walking" movements. Was breathing slowly, then stopped. The wound was opened—no bleeding found.

3:40 p. m. Marked "extensor" rigidity, clonic movements with all four legs but movements are not rhythmical.

3:45 p. m. Artificial respiration. Died.

EXPERIMENT 7.—Cat N-21-99, April 20, 1921.

3:45 p. m. Decortication. Transection through basal ganglions, 1 cm. cephalad to tentorium. (Specimen *A.*)

3:55 p. m. Cat spastic. Wagging tail.

4:00 p. m. Makes excellent alternate "walking" movements—left hind and right front leg and right hind and left front leg.

4:05 p. m. Section 5 mm. cephalad to tentorium. (Specimen *B.*)

4:10 p. m. Cat spastic. No "walking" movements. Dragged backwards while on its belly with legs extended, but makes no "walking" movements (specimen *C.*)

4:15 p. m. Transection at tentorium: head retracted; tail up; extensor rigidity.

4:35 p. m. Died.

EXPERIMENT 8.—Cat N-21-125, May 13, 1921.

3:15 p. m. Decorticated. Transection 1.5 cm. cephalad to tentorium. (Specimen *Aa.*)

3:25 p. m. Cat spastic. On stimulating the anus, waves tail back and forth, raises right hind leg and head, protrudes tongue and "licks chops."

3:44 p. m. Associated walking movements with all four legs. Raises head.

3:53 p. m. Transection 1 cm. cephalad to tentorium. (Specimen *A.*)

3:55 p. m. Associated "walking" movements—front and hind legs; raises head and neck; licked lips.

4:00 p. m. Transection 5 mm. cephalad to tentorium. (Specimen *B.*)

4:05 p. m. Marked extensor rigidity immediately. No associated "walking" movements. Transection at tentorium. Decerebrate rigidity persists. Coughs and sneezes; moves right hind leg on stimulation of anus.

4:30 p. m. Relaxed and flaccid. Respirations becoming very weak and sighing.

4:47 p. m. Died. Necropsy shows subdural hemorrhage around the medulla extending 1 cm. downwards along the cervical cord.

EXPERIMENT 9.—Cat N-21-162, July 22, 1921.

11:35 a. m. Decorticated. Basal ganglions intact. (Specimen *A.*)

11:38 a. m. Animal spastic. Wags tail and moves legs.

11:45 a. m. Attempts to rise from table; raises head and commences to move legs.

11:46 a. m. Continuous associated "walking" movements with fore and hind legs. Trotting movements also occur.

12:00 a. m. Transection at superior colliculi: cat struggles momentarily (Specimen *B.*)

Extreme extensor rigidity for ten minutes. No associated "walking" movements. Not breathing well, cannula cleaned.

12:10 p. m. Died.

EXPERIMENT 10.—Cat N-21-167, July 27, 1921.

2:30 p. m. Decorticated. (Specimen *A.*)

2:50 p. m. Slight spasticity of legs and tail. Excellent associated "walking" movements with fore and hind legs after slight stimulation of tail.

2:55 p. m. Transection 5 mm. cephalad to tentorium. (Specimen *B.*) Marked spasticity and no associated "walking" movements. Knee jerks are very active.

3:05 p. m. Transection at tentorium. (Specimen *C.*) Marked rigidity of the extensor type, tail held erect. Breathing very shallow.

3:15 p. m. Died.

EXPERIMENT 11.—Cat N-21-168.

3:58 p. m. Decorticated. (Specimen *A.*)

4:02 p. m. Cat shows slight spasticity which is more marked in the front legs.

4:07 p. m. Good associated "walking" movements with fore and hind legs.

4:10 p. m. Transection 8 mm. cephalad to tentorium. (Specimen *B.*)

4:20 p. m. No "walking" movements with fore or hind legs. Marked extensor rigidity with extreme opisthotonus. Died.

EXPERIMENTAL RESULTS

A study of the protocols shows that in a typical experiment the sequence of events is somewhat as follows:

After recovery from the first operation, (the cortex and basal ganglions back to 10 mm. cephalad to the tentorium having been removed), the animal is placed in the prone position with the fore legs directed forward and the hind legs backward (Fig. 1 *A*). Stimulation is then applied by stretching the anus, pinching the tail, or gently pulling the animal along a smooth surface so as to stimulate the ventral surfaces. Orderly alternating movements then occur; that is, the right fore and left hind leg flex simultaneously while the left fore and right hind leg are extending (Fig. 1 *B*). This act is then repeated, rhythmically, alternating, for a minute or two until more stimulation is needed.

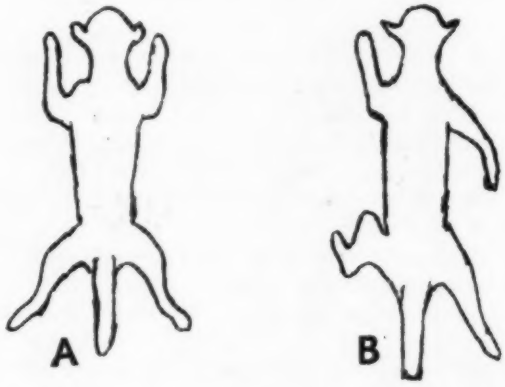

Fig. 1.—*A*, initial position of animal; *B*, limb pattern in alternating movements on stimulation.

This demonstrates the presence of a mechanism controlling the automatic association of locomotor reflexes of the right and left and the fore and hind extremities. Postural reflexes are also present in this preparation, causing enough "spasticity" in the antigravity group of muscles to enable the animal to stand when supported by the nape of the neck. When thus held, actual walking can be demonstrated, and especially active preparations can jump vigorously. Having thus observed the results of the first operation, the packing is gently removed from the cranium, the vertebral arteries are compressed as before and the basal ganglions are transected at a point about 5 mm. cephalad to the tentorium. (This point for making the transection was found after running several preliminary animals, in whom many very thin (1 mm.) sections were made, beginning at the most anterior portion of the basal ganglions and working towards the tentorium.) The specimen

removed was saved in formaldehyd solution for microscopic study and marked Specimen *A*.

Following this procedure it is observed that all alternating associated movements between fore and hind legs cease. The preparation lies quietly with increased rigidity. The next section is made at the tentorium and the slice of brain removed is marked, Specimen *B*. After this the animal goes into marked extensor rigidity. The remaining mid and hind brain tissue is saved in formaldehyd solution as Specimen *C*.

Table 1 summarizes the results of the eleven experiments given in the protocols. A study of the results here tabulated indicates that decortication or removal of the upper portions of the basal ganglions

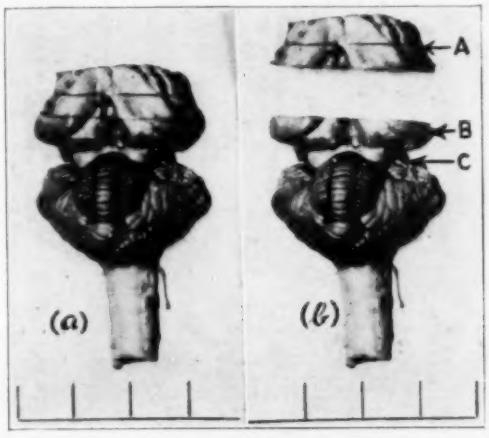

Fig. 2.—Photographs of gross specimens illustrating: (*a*) the approximate level of the first transection; (b) the approximate level of the second transection; *A*, *B* and *C* indicate Specimens *A*, *B* and *C*, respectively. The scale shown indicates centimeters.

(as far back as Fig. 2 *A*), does not interfere with the associated walking reflexes, but when the transection is made at a level as low as 5 mm. (Fig. 2 *B*), above the tentorium the movements are lost. The discrepancies found in the protocols are probably to be explained by the fact that all transections were not made at exactly the same angle; thus, structures in the subthalamic region may be present in one section and absent in another, although the dorsal parts of these sections are at identical levels. Likewise there must have been great variation in the extent of the trauma up and down the brain stem. A study of the microscopic sections shows that in some there was slight hemorrhage in the tissue, and in others about the base of the basal ganglions and midbrain.

TABLE 1.—*Results of Transections*

Cat No.	Level of First Transection	Character of Response Specimen A	Time Elapsed During Observation of Activities with Specimen A Intact	Level of Second Transaction	Character of Response Specimen B	Time Elapsed During Observation of Activities with Specimen B Intact
N-20-8.....	Cortex removed	Alternate "walking" movements	50 minutes	5 mm. cephalad to tentorium	Moderate rigidity. No alternate "walking" movements	17 minutes
N-20-12.....	Cortex and back to level of optic chiasm	Moderate rigidity of legs and tail. Alternate "walking" movements	30 minutes	5 mm anterior to tentorium	Rigid enough to stand when balanced. Alternates front legs; not all four	34 minutes
N-20-15.....	Cortex and back to level of optic chiasm	Slightly spastic. Good walking movements. Leaps into air from hind legs	60 minutes	4 mm. anterior to tentorium	No walking or running movements	21 minutes
N-21-66.....	Cortex removed	Slight rigidity of fore legs. Alternate "walking" movements	24 minutes	4 mm. caudad to first transection	Very spastic. No "walking" movements	4 hours 43 minutes
N-21-69	Cortex removed and through anterior tip of basal ganglions	Considerable spasticity. Alternate movements with hind legs. Slight movements with left fore leg	1 hour 20 minutes	At anterior colliculi	Flexion of legs. No "walking" movements	33 minutes
N-21-89.....	Cortex removed; basal ganglions intact	Makes running (alternate) and jumping movements	25 minutes	2 mm. cephalad to tentorium	Poor breathing. Artificial respiration. Extreme extensor rigidity. Died	20 minutes
N-21-99.....	Cortex removed; section 1 cm. cephalad to tentorium	Spastic. Good alternate "walking" movements	30 minutes	5 mm. cephalad to tentorium	Spastic. No "walking" movements	10 minutes
N-21-125.....	Cortex removed; section 1 cm. cephalad to tentorium	Spastic. Alternate "walking" movements	38 minutes	5 mm. cephalad to tentorium	No "walking" movements. Extensor rigidity. Died	47 minutes
N-21-162.....	Cortex removed; basal ganglions intact	Respiratory difficulty. Makes "walking" movements	25 minutes	At level of superior colliculi	Respiratory difficulty. No "walking" movements. Died	10 minutes
N-21-167.....	Cortex removed	Excellent walking movements	25 minutes	5 mm. cephalad to tentorium	No "walking" movements	10 minutes
N-21-168.....	Decorticated	Good walking movements	12 minutes	8 mm. cephalad to tentorium	No "walking" movements	10 minutes

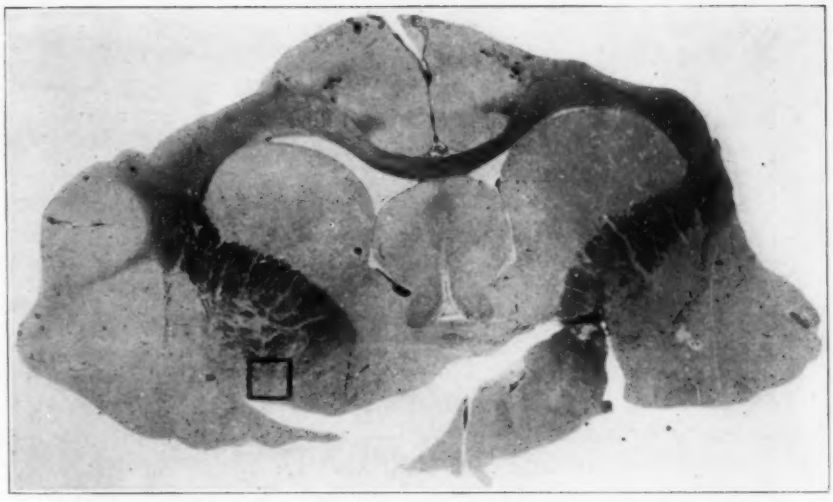

Fig. 3.—Photomicrograph of a section taken from the highest level in which centers controlling the associated locomotor movements are present. The area blocked out is that in which the characteristic multipolar rectangular cells are found. Van Heumann stain.

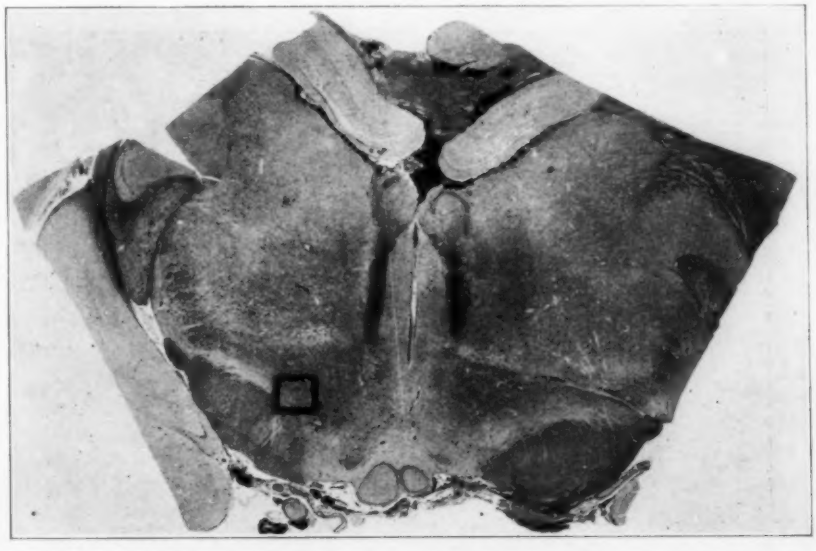

Fig. 4.—Photomicrograph of a section taken from the lowest level in which the centers controlling the associated locomotor movements are present. The area blocked out is that in which the characteristic multipolar rectangular cells are found. Van Heumann stain.

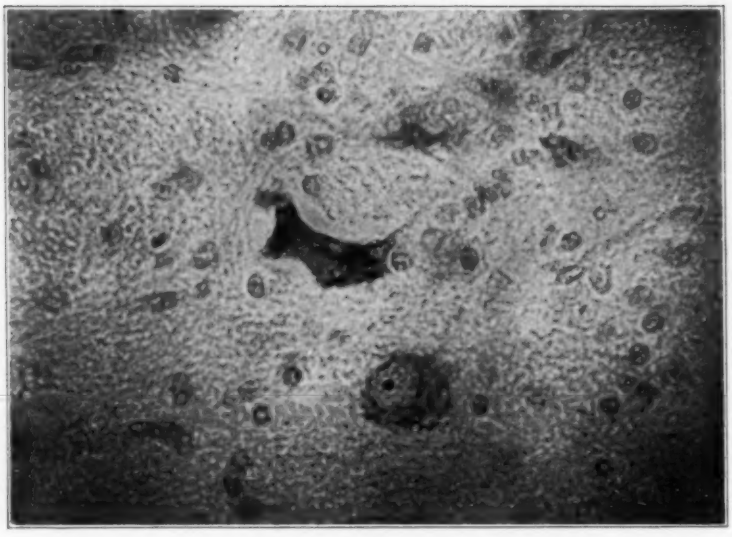

Fig. 5.—The large multipolar rectangular cell in the center illustrates the type cell characteristic of the area blocked out in Figs. 3 and 4. Cresyl-violet stain.

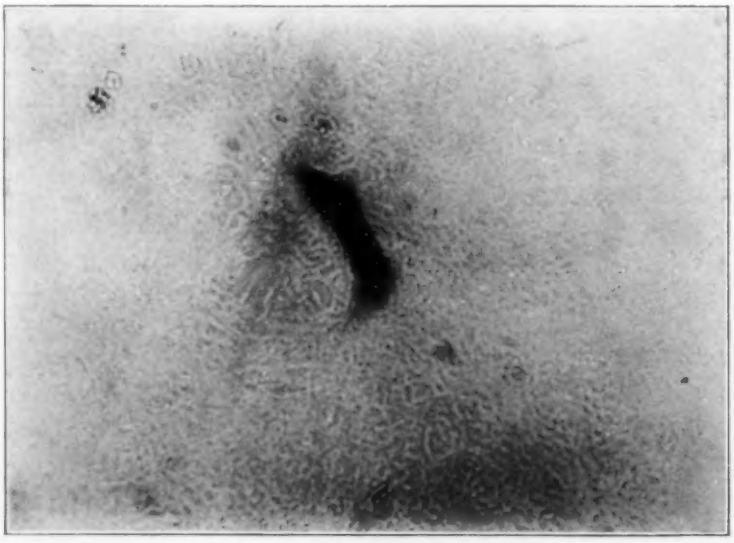

Fig. 6.—Illustrates in detail the large regularly placed Nissl bodies and location of the nucleus in the cells shown in Figure 5. Cresyl-violet stain.

In general terms, however, it can be stated that somewhere between 5 and 10 mm. cephalad to the tentorium lies a mechanism controlling these associated movements. The anatomic studies of specimens removed at the second transection (Specimen *A*), show that this area takes in parts of the striatum, pallidum and most of the body of Luys.

The ventral end of Specimen *A*, is about at the level of the first point of union between the caudate and putamen (Fig. 3) and the lower level is quite distinctly located at 5 mm. above the tentorium where the principal anatomic landmarks are the habenula with the tract of Meynert, lateral geniculate body, pulvinar and peduncles of the cerebrum, (Fig. 4). The atlas of the brain by Winkler and Potter [9] was used as a reference for orientation.

It appears then, that we can select no well recognized structure, except the body of Luys, in the region which is present in those prepa-

TABLE 2.—*Anatomical Examination*

Specimen B	Rectangular Multipolar Cells	Body of Luys	Red Nucleus	Globus Pallidus	Striatum
N-20-8	Present	Present	Absent	Present	Present
N-20-12	Present	Present	Present	Present	Present
N-20-15	Present	Present	Absent	Present	Present
N-21-66	Present	Present	Absent	Present	Present
N-21-69	Specimen lost				
N-21-89	Present	Present	Absent	Present	Present
N-21-99	Present	Present	Absent	Present	Present
N-21-125	Present	Present	Present	Absent	Absent
N-21-162	Present	Present	Present	Absent	Absent
N-21-167	Present	Present	Absent	Present	Present
N-21-168	Present	Present	Absent	Present	Present

rations showing the associative movements and absent in those not showing them (Table 2).

A microscopic study of this area, also, presents a fact of possible significance, namely, that here is found a peculiar type of cell. These large cells do not appear cephalad to section *A.;* they do appear in section *A.;* they do not appear in section *B.;* they lie slightly lateral to the body of Luys but are not found as far laterally as the pallidum.

Their resemblance to the large pallidal cells is conspicuous, in that they are rectangular and multipolar, but they differ slightly in that there is not so much swelling of the body in the region of the nucleus (Figs. 5 and 6).

SUMMARY

This series of ablation experiments on cats seems to show that in the subthalamic region is an area which, when removed, causes cessa-

9. Winkler and Potter: An Anatomical Guide to Experimental Researches on the Cat's Brain, Amsterdam, W. Versluys, 1914.

tion of the automatic, locomotor movements associating the fore and hind legs. When this area is left intact in decorticate preparations these movements are present.

Serial transections with observations on the locomotor movements, show that the area controlling this function lies from 5 to 10 mm. cephalad to the tentorium. Here the only structures found consistently are the body of Luys and certain characteristic motor cells.

DISCUSSION

Dr. C. Macfie Campbell: When you stimulate that area in which you get these movements, do the movements keep on longer than the period of stimulation, or are there only one or two movements?

Dr. Mella: We do not stimulate the area directly. After anesthesia the animals are allowed to recover, and almost any stimulation will induce the movements, such as twisting the tail, tickling the foot, or stamping on the floor. Electricity was not used.

Dr. H. R. Viets: How far, roughly, are the cells of Luy's body from the red nucleus?

Dr. Mella: Roughly I should say that they are about 5 mm., that is the least distance at which we find any cells; most of them are about 7 mm. cephalad to the tentorium. We do not find any within 5 mm. There are really very few there; probably one could pick out one or two from the sections, but they are difficult to locate as far caudad as that. In higher sections one can locate them quite readily.

Dr. Viets: In work done in Sherrington's laboratory, we made about 150 decerebrations without paying any particular attention to the level, but surely in over half of them we got automatic movements; whether we always saved the cells of which you speak I am not sure. A good many showed the red nucleus on the surface of the section.

Dr. Mella: It depends on how one makes the section. I have attempted to bear this in mind so that the angle of transection would be practically the same in all of the experiments. If this is not considered one might make the error of transecting at the tentorium above and terminate 10 to 15 mm. cephalad to it inferiorly. Of course, some of our sections were found to vary a little. We tried to have as little hemorrhage as possible. We had to make a large number of experiments before we obtained good material to study; of these we saved about twenty of the best to work on. If it is done too roughly, hemorrhage will spoil the section. There are a good many steps—the ligation of the carotid, etc., that I have not gone into. I wish to emphasize though, that the automatic associated movements of which I have spoken are not between just the fore or hind limbs, but between all four legs.

Dr. Percival Bailey: In the course of experiments on the influence of the cerebellum on decerebrate rigidity, I had an opportunity to observe some phenomena directly bearing on the presentation of Dr. Mella. These experiments were done by Dr. Frédéric Bremer in the Laboratory of Surgical Research and I had the pleasure of doing the surgical work for him. They will be found described in full in the *Archives Internationales de Physiologie*, **9**:189, 1922. He noted that a certain optimum tonus is necessary for the production of rhythmic progressive movements. Now the simplest explanation of the results of Dr. Mella would be this: as the section passes farther back, the tonus

increases above the optimum for progression reflexes and only the extensor rigidity is seen. If, however, the tonus is reduced either by chilling of the animal, slight asphyxia, stimulation of the cerebellum, or otherwise, the progression reflexes may reappear even though the section passes back of the red nucleus.

Dr. A. Forbes: I think sometimes you can get progressive alternate movements with decerebration which has passed 5 mm. in front of the tentorium. A rough decerebration at one point may cause trauma enough to knock out the functional capacity of cells a few millimeters away. In general, if you make a section at the tentorium you get motionless rigidity. You sometimes get sprawling movements after transection even pretty close to the tentorium. Just where the dividing line is I cannot say.

Dr. Stanley Cobb: One point we ought to remember; that is, that in these experiments we were interested only in the association of the progressive movements of all four legs. In spinal preparations we may have alternate movements of one pair of legs perfectly well; and in spinal preparations you may have alternate locomotor movements during periods of stimulation. In these animals, however, the alternate movements of all four legs, in a regular rhythmic progressive reflex, were spontaneous and lasted for a long period.

THE VALUE OF VENTRICULOGRAPHY

A CLINICAL EXPERIENCE BASED ON A SERIES OF FORTY CASES*

FRANCIS C. GRANT, M.D.

PHILADELPHIA

To Dandy, we owe the brilliant conception of injecting air into the ventricles, studying them with the roentgen ray and localizing intracranial lesions from the defects in the ventricular outline. While his results with the procedure have been impressive, in other hands the exact value of the intraventricular injection of air for the localization of new growths within the brain is somewhat uncertain. Although the series of cases is relatively small, nevertheless I feel that the results in some measure confirm his claims.

Forty-four ventriculograms of forty patients were made. In fifteen cases the ventriculogram findings were confirmed at operation or necropsy. In nine cases, the exposure of the suspected area failed to reveal the disease, although, from the neurologic examination and subsequent course of the case, I believe that the lesion existed in the region exposed. Of these nine tumor suspects, unverified, in six the ventriculogram placed the lesion in the fourth ventricle or aqueduct, one in the third ventricle, one in the right frontal lobe, and one deep in the motor cortex. Of these cases, five were operated on over the suspected area. In three of the cerebellar suspects, no abnormality was noted in two cases. Of these, one has since died with every symptom of a lesion in this region, one is much improved by the suboccipital decompression, and in the third at operation a marked asymmetry of the cerebellar lobes was noted for which no cause could be found on the surface in this area. This patient has improved since the relief of pressure, but is still under observation. Of the three remaining cases, one refused operation, and two were in such poor physical condition that a palliative subtemporal decompression was performed to tide them over until a more formidable procedure seems warranted. The case of suspected third ventricle tumor was so much improved by a subtemporal decompression that she refused further interference. In the frontal lobe suspect, nothing to confirm the localization was found on a most thorough examination of this area. The patient died six months later and no necropsy was obtained. The patient in whom the diagnosis of a deep motor cortex tumor was made, was operated on and a transcortical

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* From the Clinic of Dr. C. H. Frazier, University Hospital, Philadelphia.

* Presented before a meeting of the Philadelphia Neurological Society, Jan. 26, 1923.

approach failed to reveal the growth. The neurologic symptoms were so clear that I still think that the tumor is present. Of these nine cases, then, in which the diagnosis is still unconfirmed, it is believed that the ventriculogram localization of a deep-seated lesion—not necessarily a tumor—in seven is almost certainly correct. A marked degree of distension of the lateral ventricles, internal hydrocephalus, could be caused by nothing but a lesion between the third ventricle and the basilar cistern. As meningitis as an etiologic factor may be eliminated with assurance from the history in every case, the presence of an arachnoiditis extending widely over the cortex and blocking the return of the cerebro-

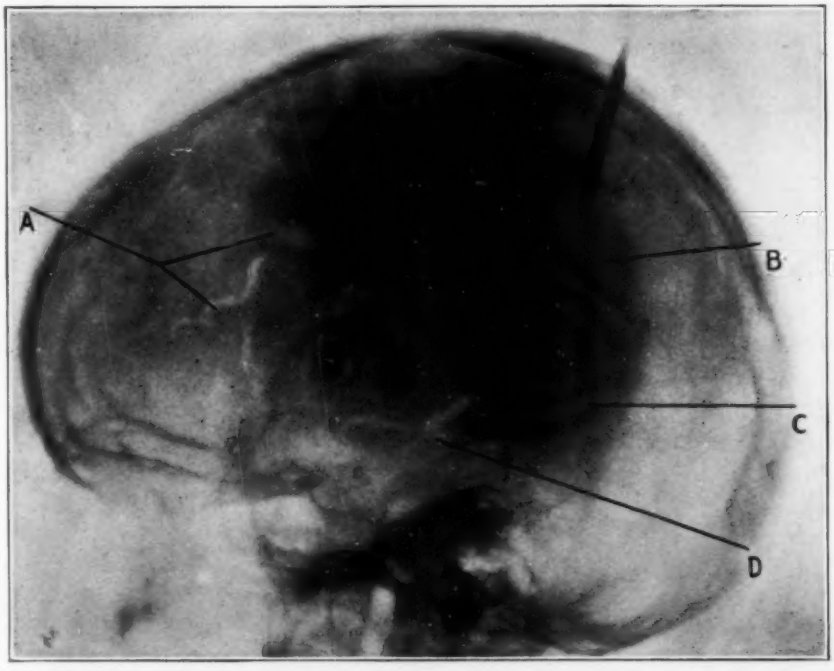

Fig. 1.—Lateral view of a normal ventricle. *A*, air in subarachnoid space; *B*, anterior horn of lateral ventricle; *C*, posterior horn of lateral ventricle; *D*, inferior horn of lateral ventricle.

spinal fluid to the great veins is unlikely. If meningitis is a factor, the adhesions have formed at the foramina of Luschka and Majendie at the base of the brain and prevent the escape of the fluid from the basilar cistern. This may have been the case in the two cerebellar exposures in which no definite lesion was demonstrable.

In the two remaining cases, the frontal lobe and motor cortex localizations, the diagnosis from the air injection may have been incorrect. The neurologic picture sustained the ventriculogram findings. At the operation, however, no lesion was revealed.

The ventriculogram led us astray in four cases of this series. Three errors in localization were later proved at necropsy. In the fourth case the air injection led us to operate in spite of negative neurologic findings. The exploration revealed nothing, although brain-puncture was resorted to in an attempt to locate a subcortical growth. This was one of the earlier cases in the series and, in the light of present knowledge, the ventriculogram would probably now have been repeated to confirm or disprove the findings before operation. Of the three cases in which the lesion was proved at necropsy to be in another area than

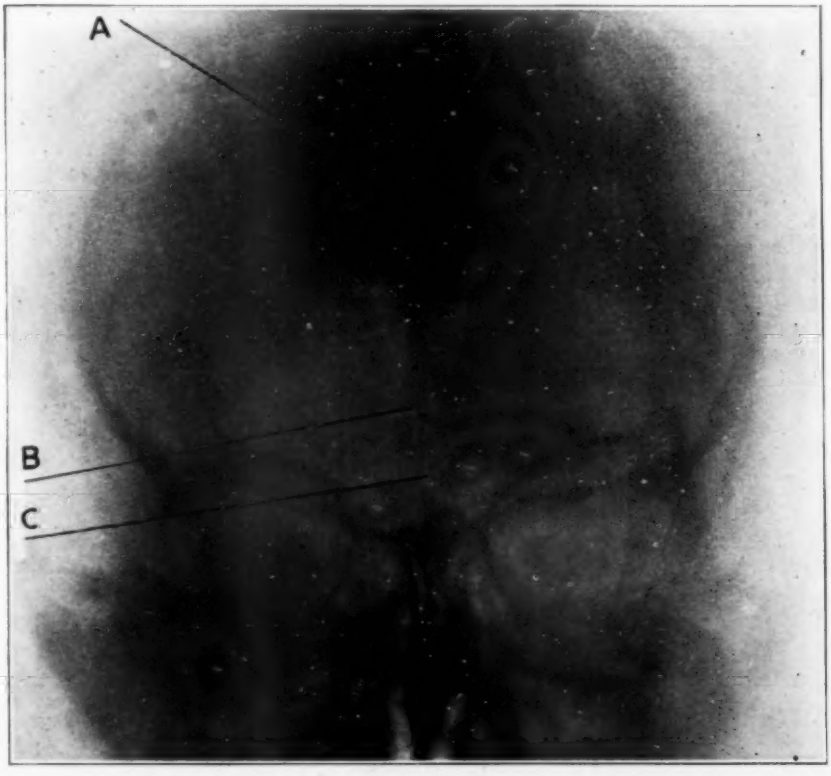

Fig. 2.—Anterior-posterior view of a normal ventricle. *A*, lateral ventricles; *B*, third ventricle; *C*, fourth ventricle.

that indicated by the ventriculogram, one was a suprasellar growth, without bone change in the sella, causing a hydrocephalus. From the visual fields it was difficult to distinguish between a lesion in this area and in the temporoparietal lobe. The ventriculogram showed a defect in the posterior horn of the lateral ventricle. The necropsy findings showed no reason for this defect; hence it must have been due to an error in the technic of the air-injection. This also was an early case in the series.

Fig. 3.—Occipital pole tumor on the left side, showing obliteration of the posterior horn on the left side. (*A*) The normal horn on the right side may be seen dimly extending into the right occipital lobe. Tumor, successfully removed at operation, was a glioma.

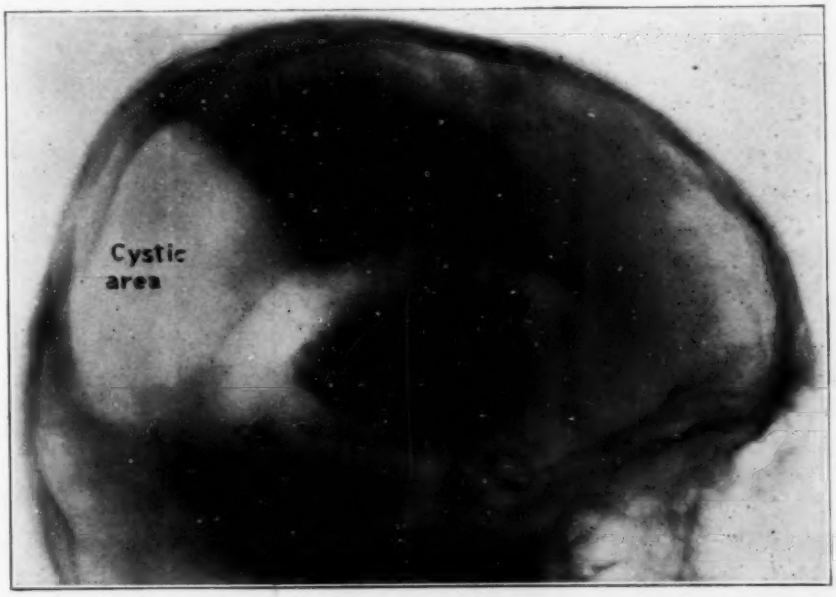

Fig. 4.—Large porencephalic cyst, springing from the posterior horn of the left ventricle. Condition confirmed at operation.

The other two cases in which the ventriculogram proved untrustworthy are most instructive. Both patients were semistuporous and the neurologic examination was of doubtful value. In one, the right lateral ventricle was tapped and a quantity of fluid evacuated with a rush. Then no more fluid escaped and it was thought that the entrance to the lateral ventricle on that side was probably occluded. The fluid was replaced with air, slightly more air being injected than the fluid

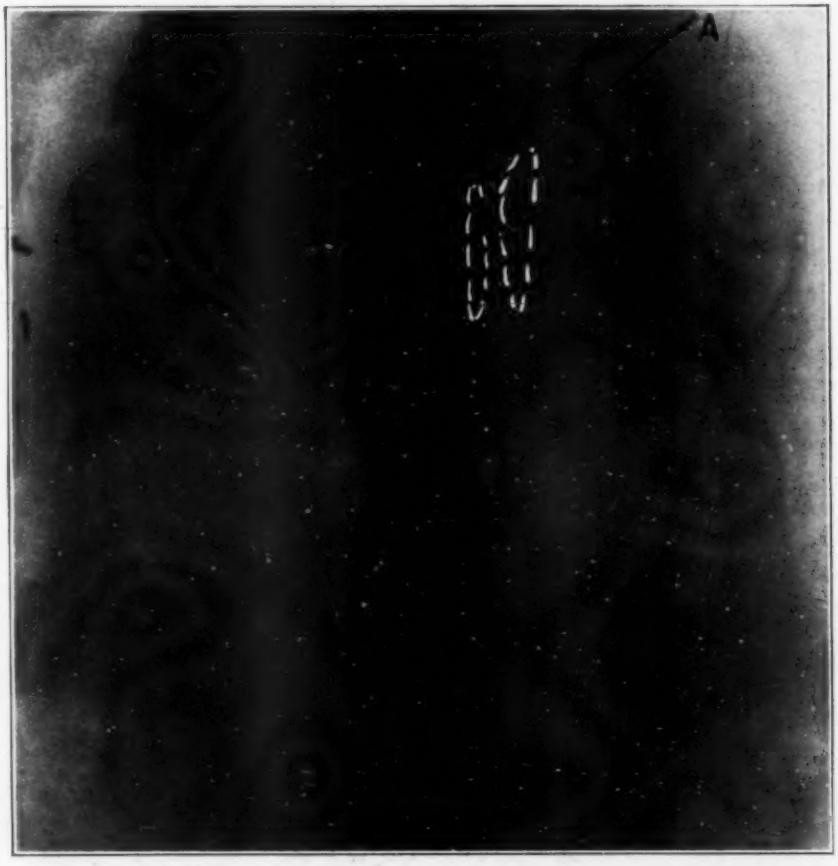

Fig. 5.—Anterior-posterior view showing ventricles pushed well across the midline by a large gliomatous tumor. Nature of tumor confirmed at operation. *A*, ventricles.

withdrawn. The roentgen-ray plates were then made and the air was allowed to escape. In order to determine whether or not the left ventricle was distended trephining was performed and an attempt was made to tap it. No fluid was obtained, but the cannula, in passing down through the brain, encountered an area of resistance that could

Fig. 6.—Anterior-posterior view showing that the anterior horn of the right ventricle *A*, is cut off on its outer aspect; and that the tumor has pushed the third ventricle somewhat to the right, *B*. Presence of the tumor confirmed at operation. The tumor was an enchondroma springing from the sphenoid bone.

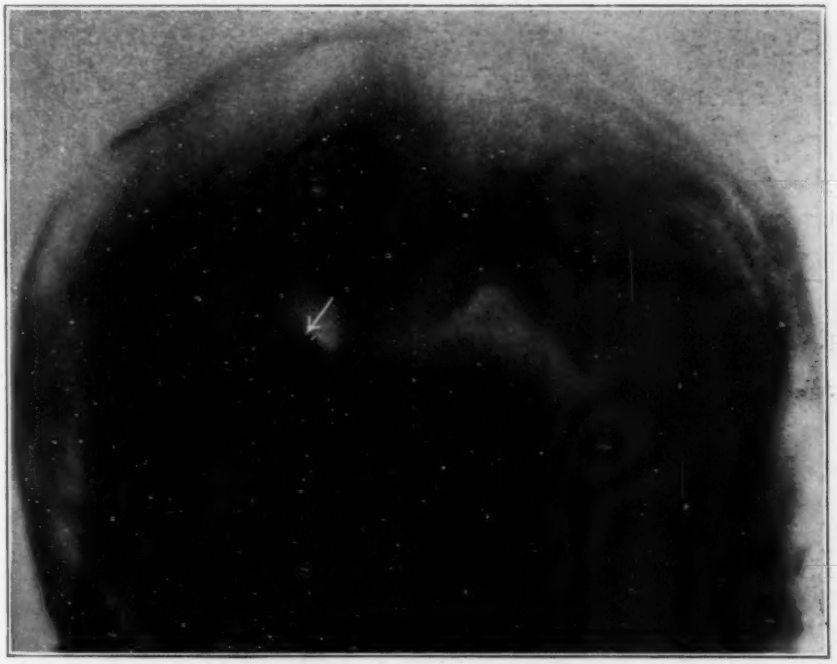

Fig. 7.—Posterior-anterior view. Both posterior horns are patulous and in normal position. Large cystic glioma found at operation entirely filling the left frontal lobe.

only be due to tumor. The patient unfortunately died following this procedure. His death may have been due either to the over-distention of the ventricular system with air, although the air was removed, or to the unexpected passage of the needle through the tumor. The roentgenogram showed that the right ventricle alone was distended with air. None had passed over into the left lateral ventricle, nor were the third or fourth ventricles demonstrable on the plate. This picture pointed to a lesion blocking the foramen of Monro on the right. Necropsy revealed that the lesion was deep in the left temporoparietal lobe, and occluded only the posterior horn of the lateral ventricle. The anterior

Fig. 8.—Anterior-posterior view; same case as Fig. 7. The left anterior horn is entirely obliterated.

horn of this ventricle was entirely patulous and apparently should have filled with air. A marked hypertrophy of the cerebrum on the side of the tumor was the only other abnormality. Whether this enlargement of the left lobe was sufficient to push the brain over to one side, compress the foramen of Monro and thus prevent the passage of air into the other parts of the ventricular system, is a matter of conjecture. In the second case the left ventricle was tapped. Again the fluid drained away in a sudden spurt and ceased to flow. We suspected that the entrance of fluid into the ventricle must be interfered with. Slightly more air was injected than fluid removed, the roentgenograms were

made and the air allowed to escape. In spite of the removal of the air, the patient developed cerebral edema and died twelve hours later. From the roentgenogram, which showed that the left ventricle alone was filled, a diagnosis was made of a deep-seated tumor obstructing the foramen of Monro on the left side. Necropsy revealed an infiltrating gliomatous tumor of the right temporal lobe involving the cortex, and at least two centimeters away from the ventricle. In no area did the tumor in any way obstruct the ventricle or impinge on it. The same

Fig. 9.—Anterior-posterior view; the right anterior horn is obliterated at its tip and pushed slightly up and to the right. The posterior part of the right ventricle may be seen lying below and slightly to the right of the normal position of the anterior horn. *A*, anterior horn of the left ventricle in relatively normal position. A large frontal lobe tumor, gliomatous in nature, springing from the base of the right frontal lobe, was found at operation.

marked hypertrophy of the ventricle on the side of the tumor was noted. In this case again the foramen of Monro may have been pushed over by this hypertrophy and compressed sufficiently to occlude it. This seems to be the only possible explanation for the misleading picture

seen in these two cases. The technic employed in making the air-injection was the same in these cases as in others in which complete distention of the whole ventricular system was obtained. In fact, the air was injected under rather greater pressure than usual, in order to obtain a clear-cut outline of the ventricles, trusting to the removal of the air to relieve the pressure and prevent a serious reaction. But had we been able to tap the other ventricle and inject it with air, the diagnosis would have been clear. The error was one of technic rather than method.

In three cases of this series, the possibility of brain-tumor in suspected cases could be excluded, because the ventriculogram showed the ventricles to be of normal contour, not enlarged and patulous throughout.

Fig. 10.—Lateral view of same case as Fig. 9, showing the anterior horn of the right ventricle, *A*, pushed up and cut off so that it does not extend as far forward as it normally should.

In one case of hydrocephalus the level of the lesion was clearly demonstrated, but the case was too far advanced to warrant any operative interference.

There have been five deaths in this series. Three were in children and two in adults. The children presented examples of large internal hydrocephalus, in one case due to an enormous cystic gliomatous growth involving both lobes and the vermis of the cerebellum, another a glioma obstructing the aqueduct and the third a tumor of the third ventricle, the position of which was determined with accuracy. The first two cases would have been entirely inoperable. In the third case the tumor might have been removed by a transcallosal approach. The cause of

death was probably too rapid drainage of the fluid from a greatly distended ventricular system. One case was stuporous at the time the ventricular puncture was performed and died in six hours without recovering consciousness. The other suffered respiratory collapse on the table and recovered when sufficient air was injected to distend the ventricles to their previous size; but even after the air was withdrawn

Fig. 11.—Anterior-posterior view in a case of cerebellar tumor. Bilateral symmetrical hydrocephalus. *A*, lateral ventricles; the third, *B*, and fourth, *C*, ventricles may be distinguished lying directly in the midline. This fact places the lesion in the midline and at the lower end of the fourth ventricle. These findings were confirmed at operation.

and part of the fluid returned, the child had severe convulsive seizures and died four days later. The child with the third ventricle tumor suddenly became stuporous three days after the air injection and in spite of a ventricular tap to reduce the intracranial pressure succumbed

in twenty-four hours. The roentgenogram accurately localized the lesion in all of these cases. Necropsy showed that, in addition to the tumor, the walls of the ventricles were the seat of minute hemorrhages. The too sudden change in the intraventricular pressure removed the support to the thin-walled veins in the ventricular walls, causing them to rupture and bleed into the ventricles. In this clinic we are very careful, with children, to withdraw the fluid slowly and replace it with air as it is withdrawn, for we have found that these cases do not tolerate well the sudden release of the intracranial tension. The other two deaths, occurring in adults, were those already referred to, in which the roentgen-ray diagnosis as to the location of the tumor was incorrect.

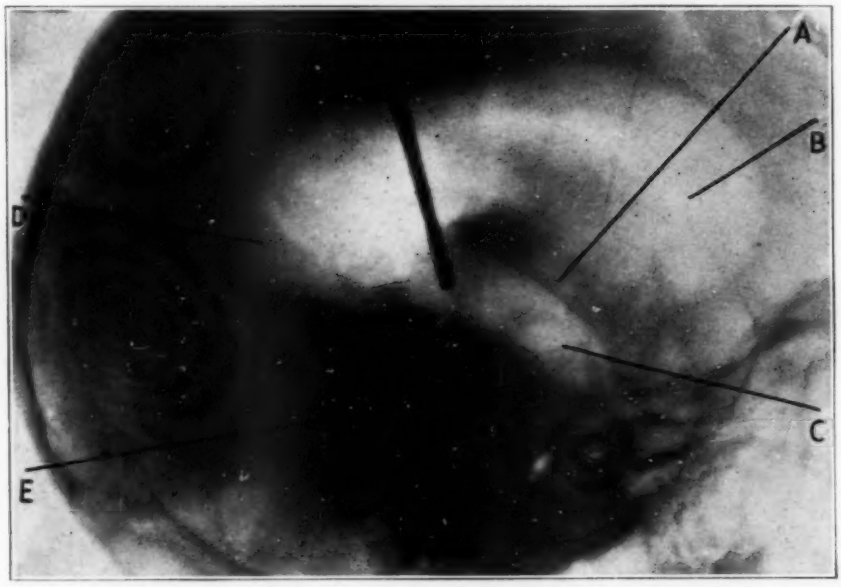

Fig. 12.—Lateral view in a case of cerebellar tumor (see Fig. 11). The tumor was a small gliomatous cyst which completely filled the lower part of the fourth ventricle. The lesion lay exactly in the midline. *A*, third ventricle; *B*, anterior horn of lateral ventricle; *C*, inferior horn of lateral ventricle; *D*, posterior horn of lateral ventricle; *E*, dilated aqueduct leading down to fourth ventricle.

Five deaths in forty cases may seem a high mortality in any diagnostic procedure, but when one remembers the mortality of unlocalized and untreated brain tumor, any method of exact localization is justifiable.

A most important step in the technic of ventriculography is the complete removal of the fluid. If all the fluid is removed the air can then pass throughout the entire ventricular system and plates from which an accurate diagnosis may be made are much more likely to be obtained. With the patient on the chest and the face turned to one

side, the skull is trephined at a point 5 cm. behind the midpoint between the bregma and the inion and 3 cm. laterad from the midline. This lies over the posterior horn of the lateral ventricle at its widest point. The cannula should be calibrated and should never pass in more than 5 cm. In all cases, except those with an internal hydrocephalus, the attempt is always made to tap and drain both ventricles. Careful manometric readings of intracranial pressure are made before and after the fluid is withdrawn and the air injected. Intracranial tension should not be increased by the amount of air injected. The air is removed subsequent to taking the roentgenograms. The fluid is only replaced in cases of internal hydrocephalus.

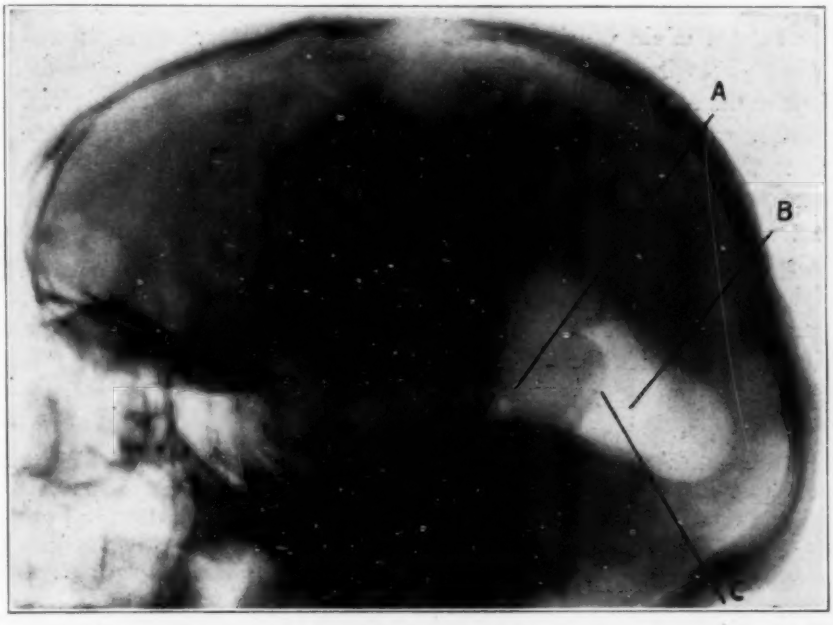

Fig. 13.—Lateral view in a case of deep-seated temporal lobe tumor impinging on the posterior horn of the lateral ventricle. Tumor removed at operation. *A*, left ventricle seen through and behind the right ventricle; *B*, right ventricle cut off by tumor which causes the filling defect at *C*.

Performing the air injection is the easiest part of the procedure. Correct interpretation of the plates is the most difficult problem. To Dr. H. K. Pancoast of the University Hospital, such measure of success as has been achieved in this clinic is mostly due. His cooperation and unflagging enthusiasm have made possible the development and standardization of our technic until we feel confidence in our localization of the lesion. Use of the Bucky diaphragm and stereoscopic plates have been of much assistance.

In conclusion, in fifteen cases, or 37 per cent., the localization by the ventriculogram was exact. In eight others, 20 per cent., the localization, while unconfirmed, seems most probably correct. In four cases, 10 per cent., the ventriculogram proved to be entirely misleading, owing to errors in technic. If two of these four had lived to have the other ventricle tapped, it might have been possible to reach a correct conclusion. In three cases, or 7.5 per cent., the possibility of tumor was excluded by this means. In three cases, 7.5 per cent., owing to an error in technic, we were not able to demonstrate the air on the roentgenogram after injection into the ventricles. One of these patients will probably have another test performed. Two patients have had a ventriculogram made and the diagnosis seems clear, but are awaiting surgical intervention. Five patients died, a mortality of 12 per cent.

In this clinic we do not feel that the ventriculogram is infallible. We do not disregard the neurologic findings if they run counter to its localization. We do not feel that every case should have an air-injection performed, particularly if the neurologic findings give positive evidence as to the area of the brain involved. But we do feel that in obscure cases or cases in which operation has not revealed a cortical growth, but where the presence of a tumor is certain, that the ventriculogram, in spite of the undoubted risk attendant on it, is a necessary and justifiable procedure. If successful, and as our experience enlarges our percentage of successes will unquestionably increase, absolute and positive information is obtained as to the location of the lesion.

DISCUSSION

DR. CHARLES H. FRAZIER: We owe Dr. Grant a debt of gratitude for the time he has devoted to the investigation of ventricular distortion. He should not be held responsible for the apparent high mortality; two of the patients of whom I asked him to make ventriculograms, were in the terminal stage of the disease at the time and as it turned out the tumor in each of these two cases was inoperable. The responsibility for the mortality in these cases I must assume. No one questions the value of the ventriculogram in suggesting the location of subcortical growths large enough to encroach on the ventricles. Virtually all of these deep seated hemispheric growths are gliomas. What we have yet to learn is this: In how many cases can these gliomas be removed in toto without sacrificing the life of the patient?

XANTHOCHROMIA AND INCREASED PROTEIN IN THE SPINAL FLUID ABOVE TUMORS OF THE CAUDA EQUINA *

HARVEY CUSHING, M.D. AND JAMES B. AYER, M.D.

BOSTON

A brief consideration of the spinal fluid abnormalities commonly associated with tumors of the spinal cord is called for as a desirable introduction to the subject of immediate interest. Our imperfect knowledge of these abnormal fluids has been acquired within a period of less than twenty years, and in this country hardly a decade has elapsed since the first paper dealing with the subject was published.

Froin [1] in 1903 first described the condition, which has become known as *"xanthochromie et de coagulation massive."* A yellow fluid which tended to clot on standing, and contained a moderate number of cells, was found in three cases of spinal disease, seemingly of subacute infectious nature, although this was not confirmed by operation or necropsy. Subsequently a number of French observers confirmed Froin's findings, especially in rare cases of chronic pachymeningitis.

In 1909, another significance was given to Froin's syndrome, as it has come to be called, by Blanchetière and Lejonne [2] who described a yellow coagulating fluid but without cell increase, below an intramedullary thoracic "sarcoma." Their observation was soon confirmed by others in cases of tumor at different levels of the spinal cord.

Our knowledge of these abnormal fluids was further advanced by Nonne [3] who in 1910 called attention to the fact that the fluid below a tumor, otherwise clear, colorless and without clot and cells, may show (his phase I. reaction) a marked excess of globulin. Nonne reported six cases, five of which were verified. In 1912, Raven [4] from

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* From the clinics of the Peter Bent Brigham Hospital and the Massachusetts General Hospital.

1. Froin, M. G.: Inflammations méningées, avec réaction chromatique, fibrineuse et cytologique du liquide céphalo-rachidien, Gaz. d. hôp., Paris, **76**:1005, 1903.

2. Blanchetière and Lejonne: Syndrome de coagulation massive et de xanthochromie du liquide céphalo-rachidien dans un cas de sarcome de la dure-mère, Gaz. d. hop., Paris **82**:1303, 1909.

3. Nonne, M.: Ueber das Vorkommen von starker Phase I Reaktion bei fehlender Lymphocytose bei 6 Fällen von Rückenmarkstumor, Deutsch. Ztschr. f. Nervenheilk. **40**:161, 1910.

4. Raven, W.: Die Bedeutung der isolierten Eiweissvermehrung und der Xanthochromie im Liquor cerebrospinalis für die Diagnose von Kompression des Rückenmarks. Erfahrungen an 15 durch Operation oder Sektion diagnostisch sichergestellten Fällen, Deutsch. Ztschr. f. Nervenheilk. **44**:380, 1912.

Nonne's clinic reported fifteen new cases and analyzed forty-seven others from the literature, concluding that it is the high protein resulting from congestion about the tumor and stasis of fluid below it which is all-important and that xanthochromia merely indicates an excessive degree of stasis.

In this same year (1912) Mestrezat [5] in his classical monograph summarized the subject to date, distinguishing erythrochromia, associated with hemorrhage, from xanthochromia accompanying massive coagulation not due to hemorrhage, although he admits for both the probability of a common origin of the coloring matter from hemoglobin. He also described the conditions deemed essential for the production of the phenomenon, namely, *a closed cavity and stasis of the fluid in the lumbar culdesac below the tumor.*

Since 1912, reports from many countries have confirmed the significance both of the "Froin syndrome" and the "Nonne syndrome." With regard to the former, two authors have recently compiled statistics of published cases, the one chiefly from French,[6] the other from German [7] sources. Both agree that xanthochromia with great excess of protein, with or without coagulation, is indicative of a space-constricting agent above the point of puncture. It is fair to say that this view, ever since its exposition by Mestrezat, has been that held by workers generally in all countries. Moreover until the observations herein recorded, it was the view held by the writers. The "Nonne syndrome" has naturally been considered a less reliable evidence of cord compression, but in the past few years the significance of this type of fluid has been greatly enhanced by tests designed to show in a dynamic manner the presence of a block in the spinal subarachnoid space.

Concerning the finding of xanthochromic fluid in the spinal canal *above* tumors, the literature is silent, although an increase of protein has been observed. Thus Marie, Foix and Robert [8] in 1913 reported an almost equal amount of protein above and below a supposed intramedullary tumor. Marie, Foix and Bouttier [9] state that below a thoracic tumor a Froin syndrome was found and that immediately above (puncture in the third thoracic space) the fluid was "five times less

5. Mestrezat, W.: La liquide céphalo-rachidien, normal et pathologique, Paris, 1912.

6. Lantuéjoul: La coagulation massive et spontanée du liquide céphalo-rachidien, Rev. Neurol. **36**:339, 1920.

7. Leschke, E.: Ueber die Gelbfärbung (Xanthochromie) der Cerebrospinalflüssigkeit, Deutsch. med. Wchnschr. **47**:376 (April 7) 1921.

8. Marie, Foix and Robert: Service que peut rendre la ponction rachidienne pratiquée à des étages différents pour le diagnostic de la hauteur d'une compression médullaire, Rev. neurol. **25**:712, 1913.

9. Marie, Foix and Bouttier: Double ponction sus-et-sous lésionelle dans un cas de compression médullaire, Rev. neurol. **27**:315, 1914.

rich in albumin," thus leaving one to suppose that the upper fluid was definitely abnormal. Klieneberger [10] found a yellow fluid rich in fibrin and showing 3 per cent. albumin below a fibroma which lay opposite the second and third lumbar vertebrae, and at operation a "water-clear fluid" above the tumor; as no examination of this fluid appears to have been made, we cannot say whether or not it was pathologic. One of us (J. B. A.) [11] has also called attention to the significance of different types of fluid obtained from the cisterna magna and lumbar sac in cases of cord tumor, both fluids being at times abnormal.

There are therefore on record a few reports of abnormal fluids obtained above tumors of the spinal cord, and the significance of the less abnormal fluid above and the more abnormal below has been mentioned. In that the few recorded cases of multiple punctures have shown a number of abnormal fluids from above tumors, it is likely that increased protein, which has been the significant pathologic finding in these cases, would be found frequently if looked for. That the protein, although pathologic in amount is much less than in the fluid below the tumor, and that the fluid is seldom yellow in color, seems also to be the rule.

Strangely enough, in the lumbar region, where multiple punctures are frequently made we fail to find that attention has been called to the presence of abnormal fluid above a tumor of the cauda equina. There are several possible explanations why this has been overlooked. The point of election for lumbar puncture, as usually advocated, is below the fourth lumbar vertebra, and this in many caudal tumors results in what is recorded as a "dry" or a "bloody tap." If the tumor is sufficiently high and lies in the region of the conus, xanthochromic fluid may be obtained from this customary site of puncture, but it is unusual for one of these tumors to lie entirely below this level. If in case of a "dry tap" another puncture is made at a higher level and xanthochromic fluid is obtained, it has been a natural conclusion heretofore shared in, apparently, by all observers, ourselves included, that the obstruction must lie above the point of puncture even though dynamic tests failed to support this view. A further explanation might be adduced in the lack of cooperation between the one who makes the puncture and the diagnostician, too frequently not the same person, for it is all too common for the latter to accept the report of the former

10. Klieneberger, O. L.: Klinischer Beitrag zu dem Erkrankungen der Cauda Equina (Erfolgreich operierter Caudatumor), Monatschr. f. Psychiat. u. Neurol. **24**:97, 1908.

11. Ayer, J. B.: Puncture of the Cisterna Magna, Arch. Neurol. & Psychiat. **4**:529 (Nov.) 1920; Spinal Subarachnoid Block as Determined by Combined Cistern and Lumbar Puncture, Arch. Neurol. and Psychiat. **7**:38 (Jan.) 1922.

without critical analysis, either as to the locus from which the fluid has been withdrawn, or as to the nature of the findings.

A few references from the literature will suffice to substantiate the above comments. Collins and Elsberg [12] in their article (1914) on giant tumors of the conus and cauda, performed punctures in two cases: one was a dry tap, the other showed xanthochromia with massive coagulation, the tumor in this case involving both conus and cauda. They dismiss the matter of the cerebrospinal fluid with the statement that "lumbar puncture was negative, or yellow fluid which was not cerebrospinal fluid was withdrawn," and in quoting the syndrome of epiconus lesions described by Minor, they say: "By lumbar puncture no fluid is obtained because the entire lower part of the spinal canal is filled by the tumor mass, although yellow fluid in small quantity may be withdrawn from the tumor." This, in all probability would not be their interpretation today of these findings, and the quotations are given merely to show what interpretation was put on xanthochromia eight years ago.

More recently (1921) Raven [13] has analyzed the fluids of 145 cases of cord tumor, including thirty-one in which the conus and caudal region were involved. His records show only one case in which the fluid was almost surely withdrawn from above the tumor, and in this case the Nonne Phase I reaction was reported as + +, but without any hint that the fluid might have come from above instead of below the lesion. In this present year, Parker [14] presents eight cases of conus and cauda tumors from the Mayo Clinic. From an analysis of his case reports, it is unlikely that the fluid was obtained above the tumor in any, but as he does not give the site of puncture this cannot be stated definitely. The abnormal fluids found by Oppenheim,[15] by Jacobsohn,[16] and by Greenfield [17] were almost certainly obtained from below high caudal tumors.

Certain cases of tumor of the cauda equina in which there is persistent pain in the distribution of the sacral nerves, stiffness of the lumbar region, loss of reflexes, anesthesia in the sacral skin fields, and

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12. Collins, J. L., and Elsberg, C. A.: Giant Tumors of the Conus and Cauda Equina, Am. J. M. Sc. **147**:493, 1914.

13. Raven, W.: Der Liquor cerebrospinalis bei Rückenmarks-Kompression, Deutsch. Ztschr. f. Nervenheilk. **67**:55, 1921.

14. Parker, H. L.: The Diagnosis of Tumors of the Cauda Equina, Conus and Epiconus Medullaris. A Report of Nine Cases, Am. J. M. Sc. **163**:342, 1922.

15. Oppenheim, H.: Ueber Caudatumoren unter dem Bilde der Neuralgia ischiadica sive lumbosacralis, Monatschr. f. Psychiat. u. Neurol. **36**:391, 1914.

16. Jacobsohn, L.: Zur Symptomatologie der Neubildungen am Conus und der Cauda Equina, Deutsch. med. Wchnschr. **38**:157, 1912.

17. Greenfield, J. G.: On Froin's Syndrome, and Its Relation to Allied Conditions in the Cerebrospinal Fluid, J. Neurol. & Psychopath. **2**:105, 1921.

a disturbance of the rectal and vesical sphincters, are easily recognized from the neurologic examination alone. However, should these symptoms be less full blown, as they are likely to be in those stages of the disorder when surgery offers a greater prospect of relief, the diagnosis, as the history of Cases 2 and 3 to be described shows, may be difficult in the extreme, and it is in such cases that the examination of the cerebrospinal fluid may be of the greatest importance.

Within the past two years, five cases verified by operation have been seen by one or both of us, in which xanthochromia and increased protein appeared in the fluid above cauda tumors. In two of these, laminectomy was performed for cord tumor, partly on the mistaken supposition that a xanthochromic spinal fluid indicated tumor *above* the point of puncture.

The first of these cases, which showed how misinterpretation of the fluid findings may lead to error in localization, was studied by one of us (J. B. A.) at the Massachusetts General Hospital.

Fig. 1.—Case 1. Tumor, intradural, opposite the second lumbar vertebra.

REPORTS AND COMMENTS ON CASES

CASE 1.—*Bilateral atrophic paralysis of lower extremities with sensory level at second lumbar segment. Operation directed to spinal cord on account of double Babinski sign, xanthochromic spinal fluid and roentgen-ray abnormalities. Cauda tumor found subsequently. Death.*

History.—Mr. LaR., aged 47, a builder, had complained for over two years of increasing pain in the lower part of the back and down the thighs and into the legs, and more recently into the feet and toes. For six months previous to examination, there had been progressive numbness and weakness of the right leg, and some difficulty in sphincter control. Examination showed weakness of both lower extremities, especially on the right, with moderate atrophy of the quadriceps, and perhaps also the glutei and calf muscles; marked diminution of all forms of sensation over the right leg and thigh up to and including the second lumbar segment, the sensory loss being most marked in the second lumbar zone; less certain sensory loss on the left; absent achilles and knee jerks on both sides; bilateral Babinski sign. Roentgen-ray examination showed proliferative changes at the margins of the eleventh and twelfth thoracic vertebrae.

Spinal Fluid Examination.—Puncture at the space between the third and fourth lumbar vertebrae yielded barely 5 c.c. of clear, yellow fluid which clotted promptly. Coagulable protein was excessive; Wassermann reaction negative.

A diagnosis of tumor seemed certain, but whether in the lumbar cord or the region of the cauda equina was debatable. In favor of the latter was the unmistakable atrophy with absent tendon reflexes. On the other hand the symmetrical bilateral distribution of symptoms, the presence of double Babinski reactions, evidence of vertebral pathology in the neighborhood of the lumbar cord, all favored a spinal cord situation.

In that the fluid showing the Froin syndrome had been obtained from the space between the third and fourth lumbar vertebrae no localization was possible from this puncture, as both possible sites of a supposed tumor must be above

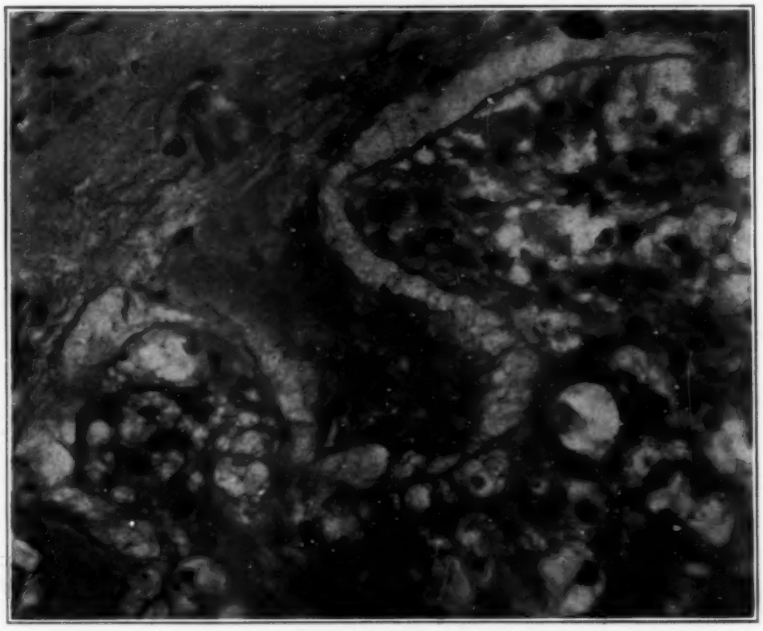

Fig. 2.—Case 2. Microscopic section of tumor: adamantinoma; medium high-power enlargement.

this point. It was, therefore, proposed to perform a puncture between these two possible sites, under the mistaken belief that if a fluid like the first were obtained, a tumor above was indicated.

While under ether, prior to laminectomy, a puncture was, therefore, made at the space between the twelfth dorsal and first lumbar spines.[18] A yellow fluid, thought at the time to be identical with that previously obtained from the third to fourth lumbar space was found. The operation was, therefore, directed to the lumbar cord, which was found to be entirely normal, except for slight yellow

18. Dissection of this region shows that although the tip of the spinal cord lies at this level, there is abundant space occupied by spinal fluid, and that therefore, in rare cases, puncture at this level is justified.

discoloration due to xanthochromic fluid which was obtained as high as the eighth thoracic vertebra. The incision was then extended downward and an intrathecal tumor (adamantinoma) was found below the conus and opposite the second lumbar vertebra (Figs. 1 and 2.)

When further studied in the laboratory, it was discovered that the fluids obtained immediately above and below the tumor were only apparently identical, the color being deeper yellow and the protein content being three times as great below the tumor, and also clotting promptly. The three fluids may be studied in Table 1.

Due largely to misinterpretation of the significance of xanthochromic spinal fluid obtained above a tumor of the cauda equina, operation was falsely directed to the spinal cord. While the tumor was eventually found at the lower level, and completely removed, the patient survived only a few days, dying presumably from the effect of the prolonged operative procedure.

TABLE 1.—*Fluids from Three Loci Obtained on Puncture and at Operation in Case 1*

	From Space Between Third and Fourth Lumbar Spines Sept. 28, 1920 (Puncture Below Tumor)	From Space Between Twelfth Thoracic and First Lumbar Spines Oct. 6, 1920 (Puncture Above Tumor)	From level of Eighth Thoracic Vertebra Oct. 6, 1920 (Obtained at Operation)
Character of fluid	Clear, deep yellow	Clear, lemon yellow	Slightly blood-tinged, pale yellow
	Clotted promptly	No clot	No clot
Total protein, mg. per 100 c.c.	2,187	720	286
Cells	Rare		
Wassermann reaction	Negative	Negative	
Amount of fluid	5 c.c. only obtainable	10 c.c. easily obtained	

In the case cited above, a diagnosis of tumor was apparent, but the localization was not obvious. In the two succeeding cases from the Brigham Hospital clinic the presence of tumor had seemed to a succession of observers from clinical investigation alone to be most improbable. The spinal fluid findings, however, in both cases served to fix the attention irresistibly to this diagnosis. It was the experience (of H. C.) with these two cases which led to a mutual discussion of the subject with the result of this conjoint report.

CASE 2.—*Periodical dysuria and backache due to massive intraspinal tumor (ependymal glioma) of caudal region associated with an anterior sacral spina bifida. Xanthochromia on lumbar puncture. Erroneous localization at first lumbar segment due to absent knee jerks. Primary negative exploration above tumor. Secondary operation with fatality.*

History.—Miss R. F., aged 10, referred by Dr. R. W. Lovett of Boston, was admitted to the Peter Bent Brigham Hospital, April 21, 1921, with the complaint

of lameness and pains in the legs and the diagnosis of anterior spina bifida. The youngest of a family of healthy children, the patient had been regarded as normal in every respect until the onset of lumbodorsal discomfort about two years before her admission. It is probable, however, that symptoms of her trouble had dated from early life. She had been a little slow in learning to walk and had always had a somewhat awkward gait. At the age of three she had a period of dysuria with cloudy urine attributed to a cystitis, and there were recurrences of these symptoms during the succeeding years. From the age of five to nine these bladder disturbances were less marked and she is said to have been active and well. The physical director in her school, however, noticed that she could not reach over to touch the floor and that she seemed somewhat weak in her legs. Little attention was paid to this.

Late in 1919, about eighteen months before entrance, she began having lumbar pain and a return of her former bladder symptoms, with urgency and frequence, but never any incontinence. These symptoms became aggravated, particularly at night, when she would be restless and complain of discomforts in her back and legs, which were usually relieved by assuming the knee-chest position. Her gait became awkward and for a time she was inclined to go on tip-toes. Of late there had been a tendency to toeing out when walking and she had been disposed to stumble.

During 1920 she was examined by a succession of orthopedists and neurologists. Numerous roentgenograms of the spine were taken which were considered as negative. One of the more recent diagnoses was of poliomyelitis, the possibility of spinal tumor having been considered and discarded.

Since early in 1921 the patient had been for a large part of the time on a Bradford frame which seemed to make her considerably more comfortable. At Dr. Lovett's suggestion further radiograms were taken, which revealed a defect (Fig. 3) in the upper part of the sacrum communicating apparently with a large, thick-walled cyst in the pelvis. These findings were supposed to represent a large anterior spina bifida with a pelvic sac, and on reviewing her earlier plates, the same conditions, though less clearly indicated, proved to be discernible in all of them.

Physical Examination.—A well-nourished child of normal mentality. The lower extremities appeared to be a little small for the body, though well formed. Her favored position was on her back, with the knees drawn up and legs separated. When the legs were straightened out the feet were rigidly extended in a position of equinus, but on flexing the knees again this position would relax and normal dorsal flexion at the ankle would be permitted. There was, moreover, a positive Kernig sign with resistance to extension of the leg beyond 90 degrees. The child could stand on her toes with the legs straight, but in walking with her heels on the ground she assumed about the attitude of a person on horseback. The quadriceps femoris on each side seemed to be weak compared to the other muscles, but there were no paralyses. Sensation on repeated and detailed tests was normal. The reflexes were peculiar in that the knee jerk could not be elicited, whereas the ankle jerks were lively with a tendency to clonus. Plantar, anal, and abdominal skin reflexes were normal. The visceral reflexes, nevertheless, were evidently impaired, to judge from the sluggish bowel movements and the tendency to retention of urine with periodic voiding of large amounts. Rectal examination was negative, and on repeating the roentgen-ray examination of the pelvis after catheterization, the large sac supposed to be the anterior protrusion of a spina bifida had disappeared.

Fig. 3.—Case 2. Roentgenogram of spine showing defect of centrum of fifth lumbar vertebra and upper sacrum (anterior spina bifida). Also, pressure absorption of laminae of fourth and fifth lumbar vertebrae.

A lumbar puncture at the third to fourth lumbar interspace showed highly colored xanthochromic fluid, which did not clot but contained an excess of protein, due possibly to the presence of a few erythrocytes. The fluid showed, per cubic millimeter, seven polymorphonuclears and three lymphocytes.

The positive findings, therefore, were: (1) a defect in the upper sacral body and lower part of the fifth lumbar centrum; (2) lumbar discomforts radiating into the thighs with absent knee jerks and apparent weakness of the quadriceps; (3) a positive Kernig sign and inability to straighten the legs without forcing the feet into an equinus position; (4) a highly xanthochromic spinal fluid.

A diagnosis was made of tumor, probably congenital (dermoid?) at the upper lumbar level[19] accounting for the lost knee jerks. It was supposed (H. C.) that the tumor must of course lie above the point of lumbar puncture.

Operation 1.—April 30, 1921, a laminectomy (ninth thoracic to first lumbar) was performed with the view of bringing the upper lumbar enlargement in view in the center of the field. Aside from the xanthochromic fluid the findings were negative. The exposure of the cord was then carried upward to the sixth thoracic by removing three more laminae, without disclosing the expected lesion. A filiform bougie was passed up the canal between dura and arachnoid, well into the cervical region without meeting with an obstruction. It was also passed down in the canal for a short distance, but as there was no suggestion in the operator's mind of a caudal lesion the search by bougie was only carried sufficiently far down to be sure that it had passed the point of lumbar puncture, only a vertebra below the exposed area.

This negative exploration was well borne and the child made an excellent surgical recovery; the preexisting symptoms remained unchanged, with the exception that it was possible after the operation for the first time to elicit her knee jerks.

A later roentgen-ray study showed that there was still sufficient room between the lowest lamina removed and the point of lumbar puncture to have possibly concealed a small tumor and still have permitted xanthochromic fluid to have been removed from below it. A secondary operation was advised but the parents begged for delay and she was taken to the country.

Aug. 26, 1921. Reentry owing to continued backache with increasing disability. There was no apparent change in her condition except for definite tenderness in the mid line over the lumbosacral junction. The deep reflexes at this time were brisk and easily elicited, and plantar response was normal. No lowering of cutaneous sensitivity could be detected anywhere over the lower sacral or lumbar skin fields.

Operation 2.—Aug. 29, 1921. The former laminectomy was continued downward and on removing the lower lumbar spines a bulging, dark, tense dura without pulsation was disclosed. Farther down in the upper sacral region, corresponding to the point of tenderness and underlying a layer of panniculus

19. This, to be sure, was high above the spina bifida, but Dr. Lawrence Reynolds, the hospital radiographer, called attention to the fact that these anterior spinal defects are not uncommon, and usually have no associated symptoms. The possible relation of tumor to the defect was therefore discounted except to suggest that, if present, it might also be of some congenital type. One of us (H. C.) some years ago had found in the lumbar region of a child a dermoid cyst producing symptoms not very unlike those described in this case.

almost 5 cm. in thickness, the tumor had largely eroded the overlying bone and was covered merely by the thinned-out posterior ligaments. From there the tumor apparently extended down to the tip of the canal.

The lower lumbar laminae which had undergone considerable pressure absorption were removed and the posterior aspect of the extensive reddish tumor mass was exposed in its full extent. It would unquestionably have been better to have reclosed the wound at this juncture and to have substituted deep radiation for partial surgical removal. However, the child was in good condition; she had tolerated the preceding and more serious operation very well; the growth proved to be a soft, comparatively non-vascular one, and the

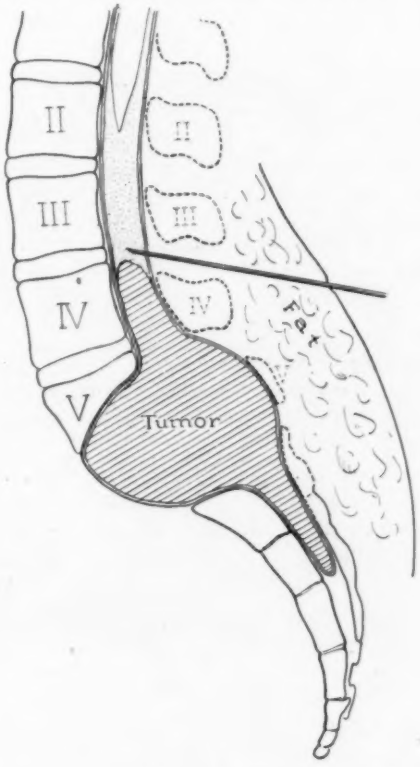

Fig. 4.—Case 2. Diagram (one-half natural size) to show approximate situation of tumor in relation to lumbar third-to-fourth puncture. Xanthochromic cerebrospinal fluid indicated by stippling.

temptation to remove as much of it as possible while it was exposed was irresistible.

Beginning at its upper portion, great masses of the tumor were easily spooned away. The lesion, however, proved to be of unexpected extent and was found to fill the cavity in the fifth lumbar vertebra, which had been previously recognized as a spina bifida anterior. On scooping the great mass of tumor out of this large pocket the soft retroperitoneal tissues were disclosed. At no time were any of the nerves of the cauda exposed. It was the operator's impression that they lay largely anterior to the growth, to judge from their disposition at

its upper pole. They must, however, have been separated by the tumor mass projecting into the defective centrum (where, indeed, the tumor may possibly have originated) and unquestionably the strands must have been subjected to considerable trauma. At all events, at this stage of the operation, though there was no special change in pulse rate, her color became poor and respiration somewhat shallow. The wound was closed. She did not revive and died before completely recovering from the anesthetic, in a condition of so-called spinal shock.

No postmortem examination was permitted, but the accompanying sketch (Fig. 4) shows diagrammatically the situation of the tumor as disclosed at the operation.

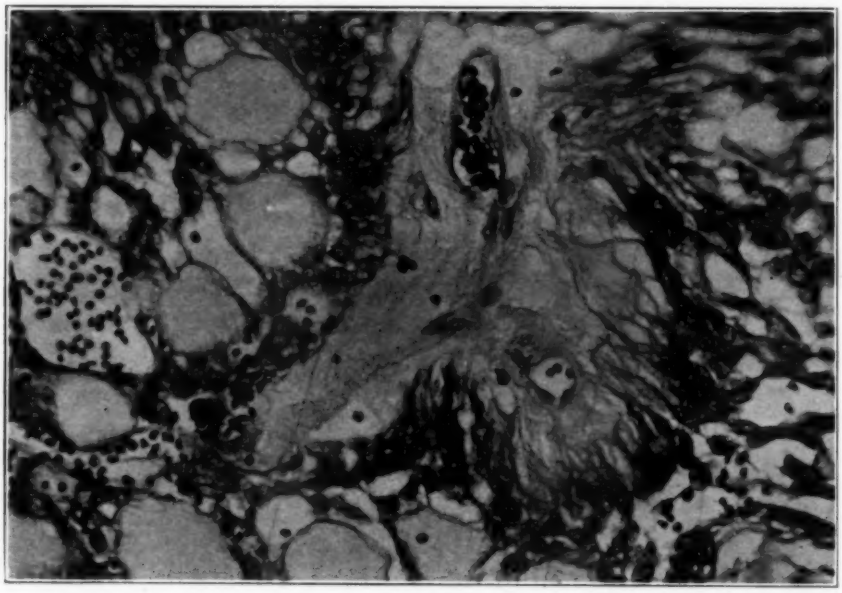

Fig. 5.—Case 2. Histopathology of lesion that was diagnosed ependymal glioma; × 300.

Pathologic Note.—A frozen-section diagnosis made at the time of the operation was reported as a possible neurocytoma or giant-celled sarcoma. A subsequent more detailed study shows (Fig. 5) a growth composed of cells with long fibrillae and a delicate connective tissue stroma with a somewhat hyalinized condition of the collagen which bears many large blood vessels. In many places the cells are elongated, tapering and lay down fibrils that stain blue in the phosphotungstic acid hematoxylin. These elongated cells extend radially from a core of the above-mentioned connective tissue. Diagnosis: Ependymal glioma.

CASE 3.—*Sacroiliac pain of twenty years' duration and obscure origin, leading to varied diagnoses and forms of treatment. Xanthochromia on lumbar puncture. Double lumbo-cisternal puncture reveals no block. Two-stage complete enucleation of large neurinoma (Verocay) compressing cauda equina. Recovery.*

Miss F. M., aged 38, referred by Dr. Muhlenberg of Reading, Pa., was admitted to the Peter Bent Brigham Hospital Sept. 19, 1921, complaining of constant pain centering in the left lumbosacral region and radiating in exacerbations down the left leg.

Past History.—Nineteen years before (1902) she fell from a bicycle, causing a painful injury to the end of her spine. Because of continued pain an operation was performed two years later in Baltimore for the removal of a tumor at the tip of the coccyx, reported to be a myxosarcoma of the type arising from a nerve sheath, and of a low grade of malignancy. The operation was a radical one of the Kraske type, with partial removal of the sacrum. Convalescence was stormy, with a cerebrospinal fluid leak leaving a persisting sinus which required a secondary operation for closure a year later (1905). There has been no local recurrence.

Her pain, which had been present since the original injury, was, however, not relieved by this operation. She became increasingly incapacitated by her discomforts and during the succeeding years was subjected to many forms of treatment by many doctors, each of whom felt confident of relieving her. As a mild degree of scoliosis had developed, most of these procedures were orthopedic and she endured a succession of casts, braces and corsets, most of which added to her torment, and in time she became what was regarded as a "confirmed spinal invalid" who needed "moral and psychic re-education."

Meanwhile she did not escape from surgical measures. A ventral suspension was performed in 1918 with a dilatation and curettement. A long period of osteopathic treatment followed. Early in the present year (1921) she had a thorough neurologic examination by competent observers in Philadelphia. As they found nothing to account for her pain, the left sciatic nerve was stretched and injected. Since this failed to give relief, the abdomen was again explored and the uterus resuspended.

Physical Examination.—An unusually dark-complexioned woman with a tendency to pigmentary deposits in her operative scars and wherever pressure had been long exerted by her orthopedic jackets. Highly keyed up, emotional, lachrymose, she complained biterly of continuous pain and sleeplessness only partly controlled by the almost constant use of narcotics.

A rectal examination with digital exploration of the pelvis was negative; there had been no recurrence of tumor at the site of her Kraske operation. There was tenderness always present over the left sacroiliac joint and a slight lumbodorsal curvature. This was revealed by the roentgenograms which were otherwise regarded as negative.

Thorough and repeated neurologic examinations gave only one positive finding, viz., the loss of the Achilles reflex on the left. This was naturally ascribed to the recent operation on the sciatic nerve. All other deep reflexes were brisk to exaggeration and the plantar response though inactive was normal. There had never been any disturbance of anal or vesical sphincters.

On one occasion only, one of the observers thought that he detected a slight relative tactual hypesthesia to hair tests in an ill-defined area around the left outer malleolus and the left perianal region of the buttock. Her feet, it may be added, were somewhat peculiar, being very small and with an abnormally high arch with the great toes held in the hammer-toe position. No muscular weakness, however, could be detected, all movements were possible, and on the occasions when she was relatively free from pain she could walk with normal gait and station.

The neurologic findings, therefore, were essentially negative except for the sacroiliac tenderness, the slight rotary spinal curvature and the inconspicuous symptoms which might have been secondary to the sciatic nerve stretching, namely, the lost ankle jerk and the slight cutaneous hypesthesia (only once detected) of the outer ankle, and to these may be added a positive Kernig sign with extension limited to 90 degrees on this same side.

An orthopedic colleague saw the case in consultation and regarded the symptoms as "functional" and attributable to her curvature. Many others had

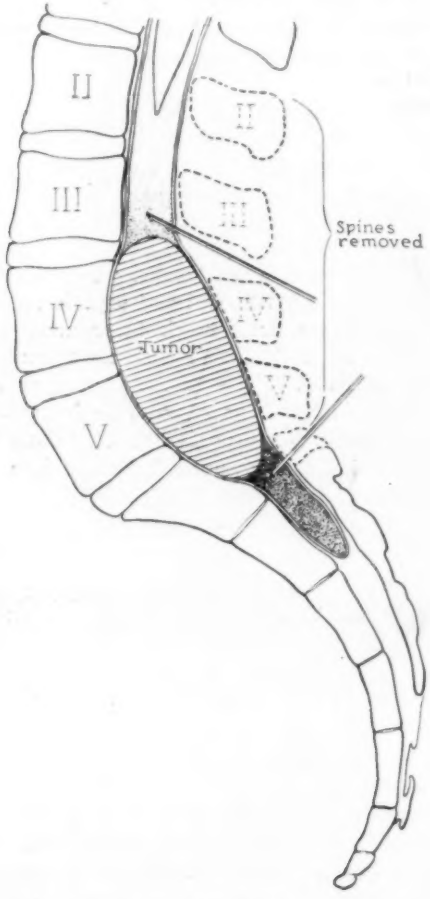

Fig. 6.—Case 3. Diagram (one-half natural size) to show approximate position of tumor in relation to fluid spaces, the degree of xanthochromia being indicated by the intensity of the stippling.

previously come to this same conclusion. To one of us (H. C.) the only suggestion of tumor in her case lay in the character of her pain and its exacerbations which were lancinating and agonizing, always in the same distribution, and brought on by change of position, and particularly by straining, coughing or sneezing. Moreover, the fact that a fibromyxoma had already been removed

from the coccygeal region, and the knowledge that these tumors when originating from nerve sheaths may be multiple, was another straw suggesting tumor.

The patient had been through so much that she rebelled at the repetition of a lumbar puncture which had been said to be negative by a previous examiner. It seemed unlikely that it would give any information of value, but she was persuaded, and on Sept. 30, a puncture was performed at the third to fourth lumbar level. The fluid had a very faint, though when compared with water, an unmistakable pale yellowish tinge. The fluid did not clot. A faint ring of globulin was precipitated by magnesium sulphate: no reduction to Fehling's solution: two cells to the cubic millimeter. Negative Wassermann reaction.

Regarding this finding as an indication of possible tumor somewhere above the point of puncture, one of us (J. B. A.) on Oct. 5th performed a combined lumbar and cisternal puncture which revealed no block, but the same faintly xanthochromic fluid as before was recovered from the lumbar needle. Com-

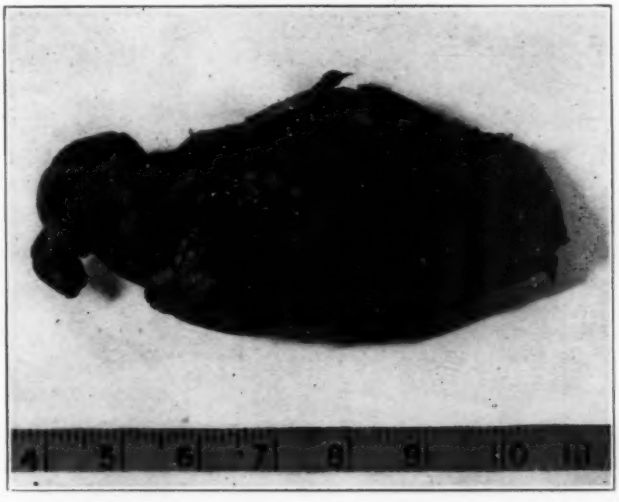

Fig. 7.—Case 3. Tumor after removal (natural size).

parison of the two fluids showed, in addition to what had been previously noted, an abnormal amount of total protein showing, with sulphosalicylic acid, 100 mg. per 100 c.c. in the cisternal fluid and 354 mg. in the lumbar fluid.

From these findings the conclusion was inevitable that there was a tumor *below* the level of the original lumbar puncture made between the third and fourth lumbar laminae. This view was supported by a subsequent tap between the fourth and fifth lumbar laminae which secured no fluid, the needle presumably entering the tumor.

Operation 1.—October 10. On exposure of the lumbar laminae, after removal of the spines, it was evident that tumor covered by dura was bulging between them. Without opening the dura, the oval growth, which extended from the upper level of the fourth lumbar lamina down to the upper margin of the sacrum, was given free exposure by complete removal of the overlying lumbar laminae, and partial removal of the posterior wall of the sacral canal. Owing to a marked fall in blood pressure, it was thought wise to reserve the attempted enucleation

for a second session. The tumor appeared to measure about 6 cm. in its vertical diameter and about 3.5 in its transverse diameter, the spinal canal being greatly dilated.[20]

Operation 2. Total Enucleation of Large Caudal Neurinoma.—October 15. On reopening the wound a needle was inserted in the meninges caudad to the lower pole of the tumor (Fig. 6) at the upper sacral margin and a small amount of highly colored xanthochromic fluid was secured which promptly coagulated on standing.

Fig. 8.—Case 3. Patient on discharge, to show situation and extent of incision.

On incising the greatly thinned and somewhat shredded dura overlying the tumor, an enucleable growth lying within the arachnoid was disclosed. The

20. After this verification of the presence of a lesion large enough to distend the lower lumbar canal, reexamination of the roentgenograms showed certain obscurations of the corresponding laminae which had not been previously regarded as signficant, though the plates had been studied by many.

nerve bundles of the cauda spindled toward the round upper pole of the tumor, most of them fortunately being disposed on its anterior and lateral aspects. Manipulation of the growth caused such abrupt lowerings of blood pressure that the nerve bundles had to be effectually novocainized before it was deemed safe to undertake the dislodgment of the snugly-fitting lesion. Fortunately the upper part of the growth contained a large cyst and after this was evacuated the tumor could be peeled away from the nerve bundles on each side and it was finally delivered intact from the greatly distended canal (Fig. 7). The flattened nerve bundles lay plastered against the dural envelope and even the bodies of the adjacent vertebrae showed molding by the growth. The cavity was filled with salt solution and the wound again closed in layers.

She made a perfect recovery (Fig. 8) and was discharged November 17 completely freed from pain, and absolutely without any symptoms except that the left ankle jerk was not regained. She remains well.

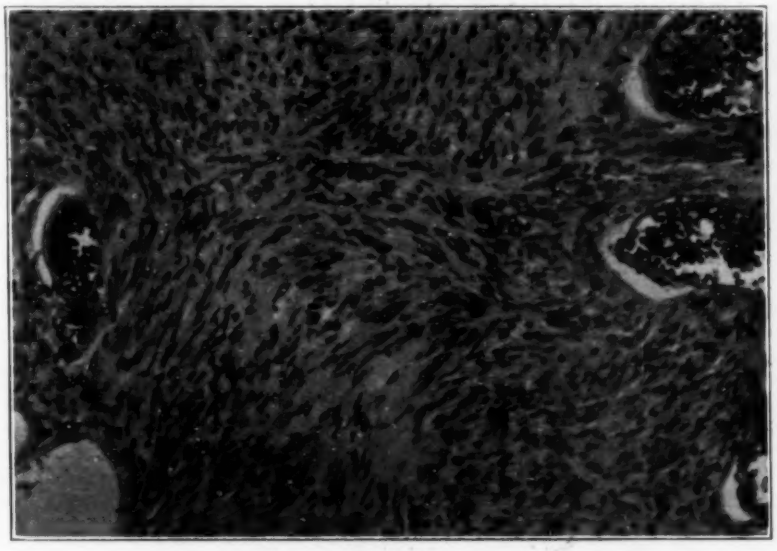

Fig. 9.—Case 3. Section of fibrous area from neurinoma; ×170.

Microscopic Report.—The tumor is composed in the main of spindle-shaped cells in bundles running in all directions. There is a very delicate fibrillary intracellular substance which stains pinkish with eosin-methylene-blue, and with phosphotungstic-acid-hematoxylin a brownish grey in contrast to the yellow brown of ordinary collagen. Portions of the growth are very vascular, and these areas, as well as other non-vascular portions, contain large round cells with finely vacuolated cytoplasm such as are commonly found in these tumors. In the spindle-cell portions a palisade arrangement of nuclei often appears. A few mitotic figures are found after patient search.

Diagnosis.—Neurofibroma of Recklinghausen type (Fig. 9).

The striking feature of these two case histories, both of them dealing with large tumors of the caudal region of many years' dura-

tion, was the obscurity of the neurologic symptoms. Both patients had been in the care of, and thoroughly examined by eminent neurologists, and apparently a spinal tumor was not suspected. Pain was the distinguishing feature of each case, a dull discomfort in the first patient ascribed to various causes; a radiating type of pain in the second ascribed to scoliosis and sacroiliac strain. Neither of them showed any of the textbook symptoms of caudal lesion in the shape of motor paralyses or determinable hypesthesias of the segmental skin fields. The visceral reflexes in the first case were affected but not in the second.

To be sure, in the first patient the roentgen rays had revealed an anterior spina bifida, but even so, without the lumbar puncture and the xanthochromia which it revealed, a spinal tumor would not have been suspected. As it was, this finding as a localizing agent was misinterpreted. In the second case, without the faint xanthochromia which might easily have been overlooked, it is doubtful whether a diagnosis of spinal cord tumor would have been ventured on at all. There is also reason to doubt whether a caudal localization in the case of Miss F. M. would have been considered had not the experience with the first of the patients, Miss R. F., made the operator sufficiently wary to suggest in the second patient that the double puncture be made so as to exclude a lesion above the lumbar puncture level.

The disclosures relating to the presence of *xanthochromia above the tumor* in both of these cases, and in the latter to the demonstration below the growth of much more highly colored fluid capable of massive coagulation were what led the authors to compare notes on the subject. Since then, each of us has observed another example of the condition, so that it cannot be at all uncommon. The following case is reported (by J. B. A.) from the Massachusetts General Hospital records, and the succeeding one (by H. C.) from those of the Brigham Hospital.

CASE 4.—*Root pains for six years, culminating in a typical picture of cauda equina tumor. Demonstration by dynamic tests that xanthochromic fluid was above the tumor.*

History.—J. T. McG., aged 42, single, formerly a motorman, for six years had done no work on account of illness. He was admitted to the Massachusetts General Hospital May 11, 1922, because of paralysis of both legs, severe pains and incontinence.

Six years before his first symptom had been pain "like a toothache" in the lower back and right hip, severe enough to cause him to give up work. Although yielding to no treatment, including a cast, worn for four months, the pain in the right leg subsided after two years, but shifted to the left hip and both legs. Three years ago the left foot "got heavy" and "fell asleep," and gradually lost power. Shortly after this he began to lose control of urinary and rectal sphincters, and since then there has been a progressive loss of strength in the

legs, so that for some time he has been able to get around only with the use of crutches. He believes that the muscles of the thighs and calves are smaller than formerly.

The only incidents of possible significance in the previous history are two accidents, one at the age of fourteen when he fell from a tree, hitting his back; the other at thirty-two when he fell from a horse, injuring the tip of his spine; no sequelae of importance seemed to follow either accident. Venereal disease was denied.

Physical Examination.—Negative. Neurologic examination showed great weakness, but without complete paralysis, in all muscles of the lower extremities. There was symmetrical moderate atrophy of the quadriceps, calves, and hamstrings. The knee and Achilles jerks were abolished but there was a slight plantar response on the right only. The record of sensory tests is not so specific as could be wished but shows that tactile, painful, and thermal sense were greatly diminished, though not abolished, below the second lumbar segment on each side.

Roentgen-ray examination showed no abnormality of the spine from the seventh thoracic to the fourth lumbar vertebra, but the fifth lumbar vertebra, while preserved in its outline, suggested a pathologic process not unlike that of malignancy. The blood Wassermann reaction was negative.

Spinal Fluid.—Although a tumor of the cauda was clinically almost certain, it was determined to check this diagnosis by spinal fluid examination. On May 12, the house officer in charge had attempted a lumbar puncture at the spaces between the third and fourth and between the fourth and fifth lumbar vertebrae and failed to obtain fluid. The reason seemed apparent, that the tumor had filled this place. In that the clinical evidence placed the height of nerve symptoms at the second lumbar level (atrophy of quadriceps) it was decided to tap above the tumor. And on May 13, a puncture at the space between the first and second lumbar laminae yielded a little orange-yellow fluid under a pressure of 230 mm. This fluid showed a great excess of protein, 1,000 mg. per 100 c.c., but did not clot in one hour. It contained two nucleated cells and 8,400 red corpuscles.[21] Dynamic tests were not entirely satisfactory, and the examiner was left undecided as to whether the fluid had been obtained from above or below the tumor or from a cyst. Although this type of fluid had been obtained previously from above cauda tumors in the three cases already described, yet this fluid was more deeply yellow and contained more protein than any of the others, and moreover, dynamic tests were not conclusive against obstruction above. It was, therefore, decided to make a more extensive differential study of the spinal fluid during anesthetization just prior to laminectomy. The following procedure was, therefore, carried out on May 19 with ease and a certainty of results, not obtainable from the single lumbar puncture alone. Needles were placed in the space between the twelfth thoracic and first lumbar and in the cisterna magna. Fluids from both loci were yellow, the upper of a much lighter hue; both contained clots on standing, and both showed marked protein increase, the cistern fluid six times normal, the lumbar fluid twenty-four times normal; there was no evi-

21. While there is a slight blood contamination here, this fluid presented xanthochromia rather than erythrochromia for the following reasons: (1) blood does not color a fluid in this way within twenty-four hours; (2) the protein content is far in excess of the amount to be expected from such a small amount of blood.

TABLE 2.—*Details of Spinal Fluid Examination on May 19, Case 4. Shows Block Below and Patent Subarachnoid Space Above the First Lumbar Vertebra*

	Cistern Puncture	Lumbar Puncture (Space Between Twelfth Thoracic and First Lumbar Spines)
Dynamic Studies:		
Original pressure	Normal and equal in both manometers	
Pulse oscillations	Normal and equal in both manometers	
Respiratory oscillations	Normal and equal in both manometers	
Jugular compression	Prompt and equal rise in both manometers	
Withdrawal of fluid	Prompt and equal drop in both manometers	
Injection of 70 c.c. of physiologic saline into epidural space via sacral hiatus	.....	Tardy rise of 30 mm. in lumbar manometer
Laboratory Tests:		
Character of fluid	Clear, faint yellow Slight clot	Clear, deeper yellow Slight clot
Cells: nucleated, per cm.	0	2
erythrocytes	138	396
Sugar, per cent.	0.058	0.032
Wassermann reaction	Negative	Negative
Total protein, mg. per 100 c.c	174	700

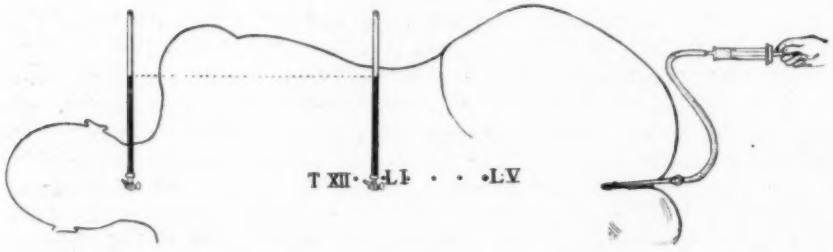

Fig. 10.—Case 4. Diagram to show needles and manometers in position for dynamic studies. No block demonstrable between cisterna magna and twelfth thoracic to first lumbar space. Block demonstrated between sacral epidural space and subarachnoid space above tumor.

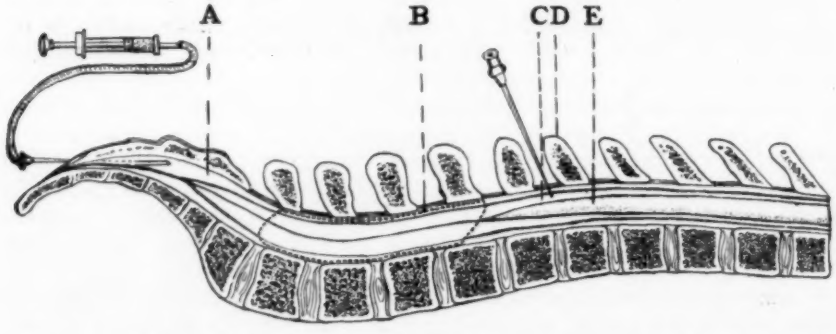

Fig. 11.—Case 4. Diagram showing method of determination of spinal subarachnoid block. Seventy cubic centimeters of physiologic saline solution injected into the epidural space by puncture of sacral hiatus, caused no appreciable rise in subarachnoid pressure above the tumor which nearly fills the sacral canal. *A*, epidural space; *B*, tumor; *C*, subarachnoid space; *D*, twelfth thoracic spine; *E*, spinal cord.

dence of subarachnoid block by dynamic tests. A needle was now inserted into the epidural space by way of the sacral hiatus, and 70 c.c. of physiologic saline solution injected. Normally with this procedure, there is a conspicuous rise in the fluid in a manometer connected with the subarachnoid space. In this case, there was a slight tardy rise only (Figs. 10 and 11, and Table 2). Punctures at the spaces between the first and second, second and third, and fourth and fifth lumbar vertebrae were now made and no fluid was obtained from any of these loci.

Operation.—At the operation (Dr. W. J. Mixter) the spinal canal was exposed from the first lumbar to the first sacral vertebra. A large soft tumor, measuring approximately 3 by 4 by 10 cm. was exposed, reaching upward as far as the conus. Partial removal only was possible, and the point of origin of the

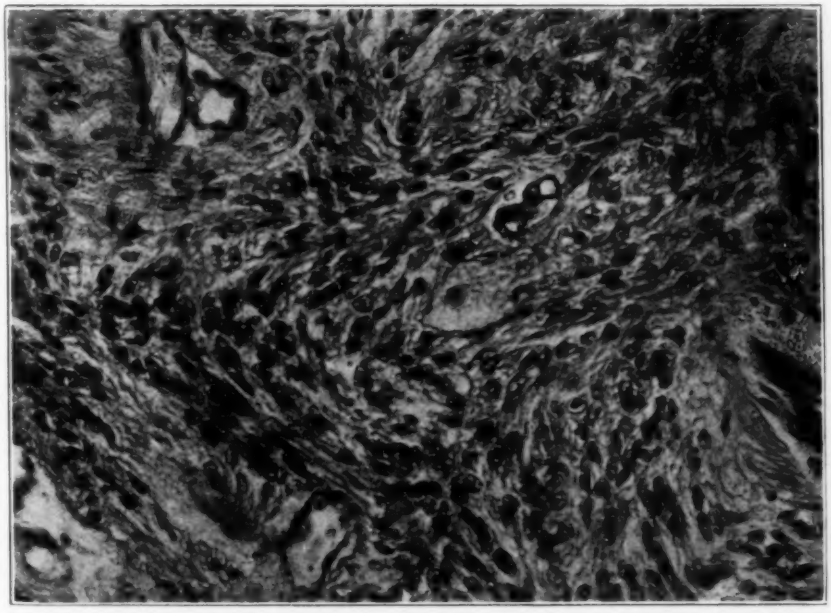

Fig. 12.—Case 4. Section of tumor. Fibrosarcoma; × 300.

tumor could not be determined. Microscopic examination showed it to be a fibrosarcoma (Fig. 12). Death occurred on the day of operation.

Comment.—In this case it was possible by means of differential punctures to confirm our clinical judgment, both as to the site and the size of a tumor of the cauda equina.

CASE 5.—*Caudal tumor of five years' duration. Xanthochromia in fluid above the tumor. Laminectomy with partial tumor removal. Recovery.*

History.—Ulric L., a French shoemaker aged 40, referred by Dr. L. R. Chaput of Haverill, Mass., was admitted to the Peter Bent Brigham Hospital, Oct. 4, 1922, as a spinal tumor "suspect" with the complaint of incontinence of urine and feces, of pain and weakness of the legs. The family and past history were unimportant except that he had had four severe attacks of inflammatory rheumatism which had left him with an impaired heart. He is the father of a family of six healthy children.

About five years ago he began to be constipated and acquired hemorrhoids for which an operation was performed. The constipation increased. Soon he noticed some loss of sensation about the lower bowel and anus, the bladder and genitals. He became impotent, his urine would dribble, and enemata were a daily necessity. At about the same time a dull ache located in these same parts began to annoy him and this ache would at times extend along the back of his legs to the feet. He had for three or four years controlled these discomforts by massive doses of acetylsalicylic acid—averaging 75 grains (5 gm.) a day and at times as high as 175 grains (11.5 gm.) a day.

He had consulted, during the five years, a great number of physicians and visited many hospitals without securing a diagnosis or getting relief. For eight months, on a doctor's advice, he had been catheterizing himself, and now has a badly infected bladder. All of his teeth were extracted on the advice of another. He had recently undergone a rigorous antisyphilitic régime in spite of repeated negative blood Wassermann reactions. On several occasions an effort had been made to get fluid by lumbar puncture. This invariably resulted in a dry tap even when undertaken under an anesthetic. Despite all this he had been able to keep at work until a few months ago, since when from pain, malnutrition and infection he had gone rapidly down hill in weight and strength.

Physical Examination.—A pale, wasted, toothless man looking much older than his years. Very poor general condition and irregular fever with daily excursions to 101 F.; hemoglobin, 30 per cent.; red blood cells, 2,500,000; marked inappetence; weight 127 pounds against his normal of 175 pounds. A serious cystitis with dribbling and 800 c.c. of residual urine. An advanced pyelonephritis; pyelograms showed a greatly dilated pelvis of what appeared to be a low horseshoe kidney. Phthalein excretion 10 per cent. in two hours.

Neurologic Studies.—Showed an almost total anesthesia of the third sacral skin-fields and below: also slight impairment over the second lumbar skin-area on the left. Toneless vesical and anal sphincters; some flaccidity of the gluteal muscles. A bed sore at the end of the sacrum; marked tenderness to pressure over the lower lumbar and sacral spines. No definite motor paralyses though considerable loss of strength in legs. Patient walked well though with pain, which was chiefly referred to the perineum and radiated down the back of the legs.

The roentgenogram of the lower spine showed an evident pressure involvement of the fifth lumbar lamina as well as of the entire sacral canal, which gave an appearance suggesting a chondrosarcoma. Rectal examination was negative.

The several punctate scars of the previous negative efforts to perform lumbar punctures were apparent, all lying between the third and fourth, the fourth and fifth lumbar spines. Since these taps had been made within two weeks of admission, some days more were allowed to elapse before a puncture was made so that the fluid might become cleared in case there had been some extravasation produced by these measures.

A needle introduced between the second and third lumbar spaces secured a light canary-colored fluid containing 3 cells per cubic millimeter and showing to alcohol ++ protein and a reducing substance to Fehling's solution. Wassermann reaction negative.

The patient was evidently in no condition to undergo an operation. Continuous bladder drainage was instituted and in the course of a month he improved greatly. He gained 15 pounds in weight, the hemoglobin rose to 60 per cent. and the reds to 4,000,000.

Operation.—December 5. The lumbar puncture at the second to third lumbar level was repeated and gave the same pale xanthochromic fluid as before, containing 8 mononuclear cells per cubic millimeter. No clot occurred on standing twenty-four hours. Total protein content was 667 mg. per hundred cubic centimeters (sulphosalicylic acid quant.). Globulin ++ and sugar 0.057 mg. per cent.

Ten cubic centimeters of this fluid were removed and a novocain solution reintroduced, but the resulting anesthesia proved insufficient and recourse had to be made to a general anesthetic (ether).

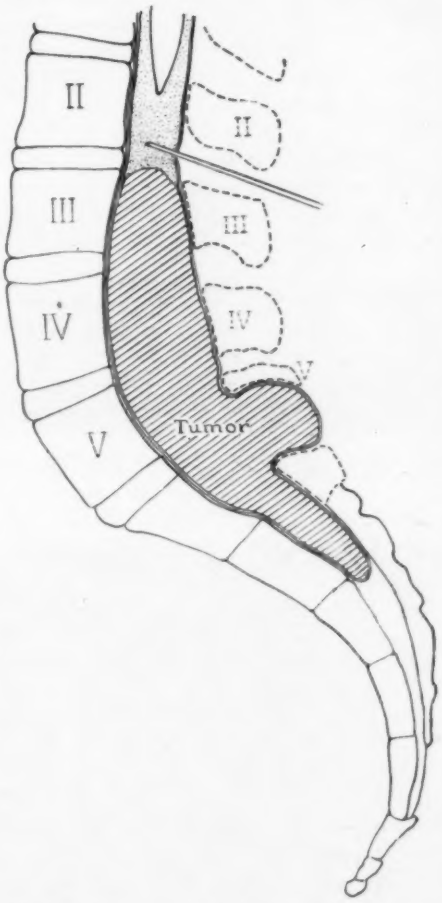

Fig. 13.—Case 5. Diagram (one-half natural size) to show approximate situation of tumor; xanthochromic fluid indicated by stippling.

A median lumbosacral incision came down on a mass of tumor the size of a hen's egg which was protruding from the canal between the fifth lumbar spine and the upper sacrum where was the chief point of tenderness. Tumor was also apparent between the thinned laminae of the third and fourth and fourth and fifth vertebrae (Fig. 13). The growth was soft, relatively non-vascular, and was surrounded by so much fat that on first impression a lipoma was sug-

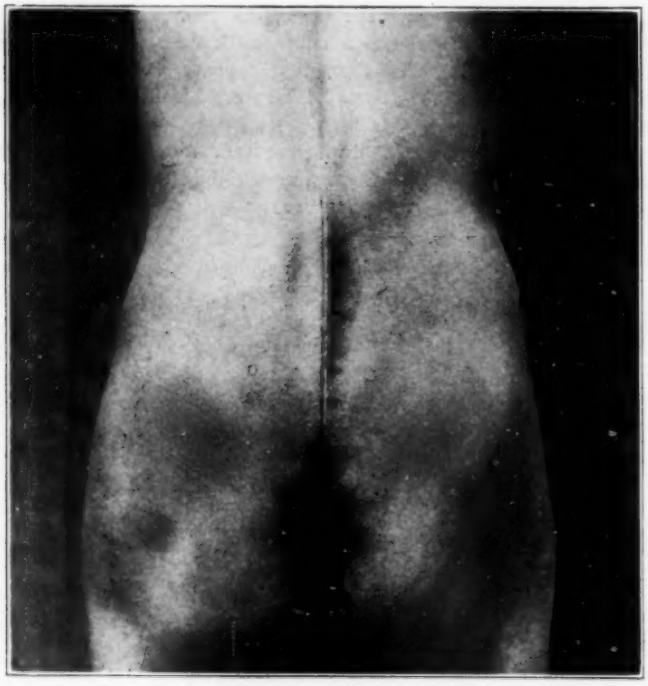

Fig. 14.—Case 5. Situation of incision that disclosed the tumor.

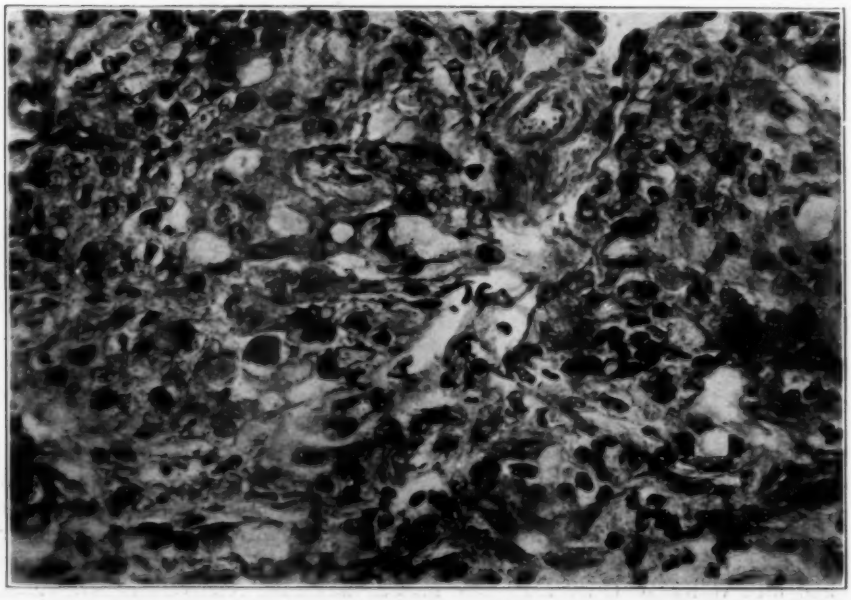

Fig. 15.—Case 5. Section of lesion diagnosed glioma; × 300.

gested. On removing the laminae and opening the greatly distended sacral canal a massive growth was disclosed, the major portion of which was scooped away and the wound closed.

Postoperative Note.—The patient made a good operative recovery (Fig. 14) with considerable relief from pain and some restoration of bladder function, though the segmental paralyses from the third lumbar downward remained largely unaltered. He was given a series of deep therapeutic radiations and was discharged Jan. 26, 1923.

Pathology (S. B. Wolbach).—Sections from all parts of the tumor show a similar histologic picture which is that of a rather loose-textured, large-celled, new growth infiltrating a dense hyaline connective tissue structure. The connective tissue occurs in places as bands having much the density of dura or periosteum. In other places it consists of small masses of hyaline-collagen material completely surrounded by tumor cells and widely separated by them. . . . In one section (probably from the protruding portion of the tumor) there is fat and muscle, the former appearing to be invaded by new growth. With eosin and methylene blue the arrangement of the cells suggests a dural endothelioma, an appearance enhanced by the concentric arrangement of cells applied to collagenous centers. But the tumor cells for the most part have a spindle shape and bear considerable resemblance to those of Case 2. With the phosphotungstic-acid-hematoxylin stain it is possible to demonstrate deep blue fibrils which are wavy and resemble neuroglia (Fig. 15).

Remarks.—"For the purposes of cataloguing (Dr. Wolbach adds) this tumor will be entered under the diagnosis of glioma. It is consistent in histology with some of the diffuse gliomas of the surface of the cerebellum and cord. I am inclined to think that the favored diagnosis, were this tissue submitted to a group of pathologists, would be endothelioma. My diagnosis of glioma is based on similarities with better-established cases and the presence of fibrils in many parts of the tumor."

GENERAL DISCUSSION

The authors are in complete agreement as to the essential fact presented in connection with these five cases—namely that *there is frequently to be found above tumors of the cauda equina a markedly pathologic spinal fluid.* It may be assumed, moreover, that intrathecal tumors found in any part of the spinal canal cause alterations in the fluid, above as well as below the lesion. Our opinions are somewhat at variance only as regards the provocative factors of the abnormality.

It is evident that in obscure cases of lumbosacral discomfort, as exemplified by Case 3, a pathologic spinal fluid may be the one significant finding which unmistakably calls attention to a lesion involving the cord. It is equally evident that the fluid abnormality has no relation to the nature of the tumor, for the histogenesis of the lesion was different in each of the five cases, the only common factor being that the tumors were all intrathecal, and were therefore directly exposed to surface contact with the fluid.

The abnormalities found in the fluid taken from above the tumor in these five cases represent what is usually considered an incomplete

Froin syndrome. In our experience, as in that of many writers, such pathologic fluids are frequently found below tumors of the spinal cord, and, until recently, have been considered, apparently by all, as indicative of some space-constricting process above the point of puncture. According to the theory of transudation into a closed cavity as advanced by Mestrezat, this is the only logical conclusion. In the cases under consideration we must therefore admit some other factor at work. One of us (J. B. A.) in agreement with Mestrezat,[5] Sprunt and Walker [22] and others is inclined to ascribe the fluid changes in the upper fluid, likewise, to transudation from the engorged veins in the spinal canal. The other of us (H. C.) attributes the fluid changes both above and below the block to direct transudation into the fluid from the surface of the tumor itself, and believes that all tumors which are subarachnoid and are bathed by cerebrospinal fluid (like the acoustic tumors for example) are accompanied by some degree of xanthochromia, though it may not be detected in fluids remote from the situation of the tumor.

However this may be, we agree that, whatever their source, the products of transudation poured into the canal below the lesion are trapped and become concentrated, whereas those above the lesion are able to escape by the normal channels of exit for the fluid, since this portion of the subarachnoid space remains open to the rhythmic variations in pressure due to pulse and respiration. Such a conception explains the fluid abnormality of less degree, with the attenuation of pathologic changes the farther one goes above the tumor. The specimens obtained by multiple puncture in Case 1 gave evidence of this, as also in Case 3 in which a stagnant pocket of highly xanthochromic fluid with clotting characteristics was disclosed at operation caudad to the growth.

Granting that a pathologic fluid is found above as well as below a tumor, what means have we for distinguishing the site of the obstruction? The difference in intensity of color and quantity of protein in the fluid above and below a tumor immediately suggests as one possible method of localization the examination of fluid from different loci of the subarachnoid space. This is a matter which has received scant mention in English and American writings, though, as stated, it has been touched on by a number of French investigators. Another differential point is seen in the quantity of fluid obtained above and below the tumor. In Case 1, for example, only 5 c.c. of fluid was obtained below, while above, 10 c.c. was easily obtained and the needle was withdrawn while fluid was still flowing. The same would have been

22. Sprunt and Walker: The Significance of Xanthochromia of the Cerebrospinal Fluid, Johns Hopkins Hosp. Bull. **28**:80, 1917.

true in Case 3 had it been possible before the operation to enter the canal below the lower pole of the tumor as well as above its upper pole.

There are, in fact, a number of ways in which one may distinguish between fluids secured above and below the lesion. For example, the pressure is less below the tumor, and if a manometer is used, respiratory and cardiac excursions are feebly, if at all, evident. Again, if a pathologic fluid in large amount is obtained from above the tumor and it is subdivided as it flows, the first fluid will show more marked changes than the later specimens which are taken. But unquestionably the criterion on which most reliance may be placed is the demonstration of the presence or absence of subarachnoid block by the use of the manometer.

It has been shown by one of us [11] that in cases in which a xanthochromic fluid with protein excess is found—and even in less abnormal fluids—in the canal below a tumor, a 'block' in the spinal subarachnoid space is usually demonstrable by means of combined cistern and lumbar puncture with accompanying manometric studies. It has also been observed independently by Queckenstedt [23] that absence of rise in lumbar pressure on jugular compression denotes 'block' above the needle. If, then, a fluid indicating transudation as in Case 3 yields normal dynamic tests it is a fair assumption that there is no obstruction above the needle, but that the source of the abnormal transudate is below the point of puncture. In suitable cases further dynamic studies may be employed, as in Case 4, to demonstrate a block between the epidural space below and the subarachnoid space above the tumor.

CONCLUSIONS

The diagnosis of caudal tumors on the basis of their neurologic symptoms alone is not always an easy matter. The determining factor may be the cerebrospinal fluid findings.

It is well known that the fluid caudad to a tumor shows marked pathologic changes generally attributed to stasis and transudation into a closed cavity, but we find that similar changes though of less degree are present in the fluid cephalad to the tumor. In the five cases reported, these fluids have all shown, in common, xanthochromia and excess protein in the practical absence of nucleated cells.

If cognizance is not taken of this fact and if the dynamic reactions of the fluid from multiple punctures are not properly interpreted an erroneous idea of the localization may lead to a futile operative search for the lesion.

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23. Queckenstedt: Zur Diagnose der Rückenmarkskompression, Deutsch. Ztschr. f. Nervenheilk. **55**:325, 1916.

CONCUSSION OF THE SPINAL CORD

A CASE WITH THE CLINICAL PICTURE OF AMYOTROPHIC LATERAL SCLEROSIS *

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Spinal cord lesions after injuries are usually indirect phenomena and secondary to fractures, dislocations, distortions of the vertebrae (Kocher [1]), rupture of the intervertebral cartilages or ligaments, meningeal and intraspinal hemorrhages. In many cases, a trauma, such as a blow, fall or shell explosion affects the spinal cord directly, producing structural nerve changes without the intermediation of the foregoing factors. Such cases are termed concussion—a condition in which, as emphasized long ago by Obersteiner [2] and Schmaus,[3] a "direct destructive action on the specific nerve elements obtains." In the majority of traumatic spinal cord lesions both direct and indirect factors are at play. For instance, the cervical region may be affected by a fractured or dislocated vertebra (indirect or intermediary action), the thoracic or lumbar regions exhibiting evidences of so-called concussion, a direct effect of the jarring of the spinal cord brought on by a trauma.[4]

The clinical phenomena, in all these pathologically different varieties, may be alike and extremely polymorphous. They may be those of myelitis, multiple sclerosis, syringomyelia, spinal muscular atrophies and even of amyotrophic lateral sclerosis. The latter was present in the case here recorded.

REPORT OF CASE

A married man, aged 60, a laborer with a good personal and family history, entered the neurologic service of Cook County Hospital Sept. 21, 1921, com-

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* Presented before the Chicago Neurological Society, January 18, 1923.

* From the Division of Neurology of the College of Medicine of the University of Illinois and the Pathology Laboratories of the Illinois State Psychopathic Institute and Cook County Hospital.

1. Kocher, Theo.: Die Läsionen des Rückenmarks bei Verletzungen der Wirbelsäule, Mitteil. a. d. Grenzgeb. d. Med. u. Chir. **1**:481, 1896.

2. Obersteiner, H.: Ueber Erschütterung des Rückenmarks, Wien. med. Jahrb. 1879, quoted by Bickeles; Obersteiner's Arb. **3**:102, 1895.

3. Schmaus, H.: Beiträge zur pathologischen Anatomie der Rückenmarkserschütterung, Virchow's Arch. f. path. Anat. **122**:326 and 470, 1890.

4. Roussy and Lhermitte: La forme hémiplégique de la commotion directe de la moelle épinière, Ann. de. méd. **4**:458, 1917. These authors classify the last mentioned group as indirect, the first as direct, spinal cord lesions.

plaining of weakness in both upper extremities. He remained in the hospital but one day and was discharged by my interns with the diagnosis of progressive muscular atrophy. He was readmitted to the hospital, in the surgical service of Dr. Besley Oct. 11, 1921 and was discharged Jan. 5, 1922, with the diagnosis of an old fracture of the cervical region of the vertebral column. March 1, 1922, he entered the Swedish Covenant Hospital where he underwent laminectomy (Dr. Roberg) and was discharged unimproved April 5. Two weeks later he died from bronchopneumonia. The facts pertaining to the history and the physical condition of the patient are given here from the history sheets of the Cook County and Swedish Covenant Hospitals.

History.—Nov. 3, 1920, the patient tripped on a wire and fell, striking the right shoulder and almost "going head over heels." He evidently did not lose consciousness for he got up and went to work, though he felt sharp pain in the "upper spine." About four weeks later he noticed weakness in the right hand; five months after the injury, there was weakness in the left hand, and eleven months after the accident the legs became weak. The weakness was accompanied by wasting and some difficulty in walking (he could not run up stairs or walk rapidly). There was no complaint of pain, headache, vertigo, gastro-intestinal, genito-urinary, deglutition, speech or visual disturbance.

Examination.—Sept. 21, 1921, examination revealed: decayed teeth in the lower jaw; absence of deformities of the vertebral column and extremities; no signs of injury to the scalp; no trophic disturbances such as bed sores; vasomotor disturbances in the hands, especially the right, which appeared red. The upper extremities, especially the right, revealed marked atrophy of the small muscles of the hands (thenar, hypothenar and interosseal), forearms and upper arms with involvement of the deltoids, supraspinati, infraspinati, serrati magni, and biceps muscles. The flexion and extension movements of the fingers, wrists, forearms and shoulders were possible, but greatly limited and weak; pronation and supination were good, but the opposition movements of the right thumb could not be carried out.

The cranial nerves were all normal; atrophy of the tongue, uvula, soft palate and lips, as well as fibrillary twitchings, were absent. The pupils were equal, round, and reacted normally to light and in accommodation. The tendon reflexes were all present, with positive Babinski, Oppenheim, Chaddock and Gordon signs, but with no clonus. One history (Nov. 26, 1921) recorded "a suggestive Babinski" and the presence of a mild clonus. The abdominal and cremasteric reflexes were present. Sensibility was normal throughout.

The blood pressure was: systolic 165, diastolic 130. The spinal fluid showed no abnormalities. The Wassermann test was negative in blood and spinal fluid. The lungs, heart, urine, temperature, speech, gait and mentality were all normal. Roentgen-ray examination at the Cook County Hospital, Sept. 21, 1921, revealed "an osteoarthritis of the sixth cervical vertebra," but no evidence of an old fracture or dislocation.

The diagnosis lay between amyotrophic lateral sclerosis and trauma of the vertebral column secondarily involving the spinal cord. For two months the patient had been treated in Dr. Besley's surgical service of Cook County Hospital by extension of the head, but without results. Extraction of the teeth was advised, but the patient refused to permit it and left the hospital Jan. 5, 1922. On March 1, he entered the Swedish Covenant Hospital, in the service of Dr. Roberg. The condition was as already recorded, but the weakness of the arms had progressed so far that the patient could not "use" them, and was "unable to care for himself." The legs were "slightly weak" and showed mild wasting.

The muscles of the right arm were somewhat more atrophied than the left; Babinski, Oppenheim and Chaddock phenomena were absent; the biceps, triceps and wrist reflexes were also absent on both sides; the roentgen-ray examination revealed a questionable fracture in the fourth and fifth cervical vertebrae with an "apparent thickened callus formation pressing on the neural canal."

In the presence of such findings and the history, Drs. Peter Bassoe and Lewis J. Pollock interpreted the condition as pressure on the spinal cord by a callus formation of the fourth or fifth cervical vertebra, though the possibility of amyotrophic lateral sclerosis was carefully considered.

Dr. Roberg performed laminectomy on April 5, 1922. He found no evidences of fracture or dislocation nor of a dural lesion, except a line of roughening on the inner aspect of the lamina of the fourth cervical vertebra. The patient survived the operation, but left the hospital unimproved and two weeks later succumbed to pneumonia.

Fig. 1.—Eighth cervical segment. The right ventral horn is somewhat smaller, contains very few, if any, myelinated fibers, the entire horn, including the lower half of the posterior horn, appearing pale and homogeneous. The right crossed pyramid including the lateral limiting zone (the angle between the anterior and posterior cornua) shows marked degeneration. The anterior pyramids do not show any changes. Weigert-Pal x 9.

Macroscopic Examination.—The gross appearance of the spinal cord delivered to the laboratory in a 10 per cent. solution of liquor formaldelhydi was perfectly normal. The meninges showed no adhesions, hemorrhages or other abnormalities. Nor were there, as Dr. Roberg informed me, any gross changes in the vertebral column (fractures, dislocations, deformities, etc.).

Microscopic Examination.—Sections stained by the Weigert-Pal method (Fig. 1) showed diminution in size of the right ventral horns, with poverty in myelinated fibers, degeneration of a large portion of both lateral (especially of

the right) columns, intactness of the anterior and posterior columns and of Flechsig's tract. Stained with the method of Alzheimer-Mann (methyl-blue eosin) the ventral horns of the lower cervical region (Fig. 2) revealed an extensive, rather pale area extending into the base of the posterior cornua, reaching in some instances to their necks. The pale area, as Figure 2 shows, appeared as if invested by a marginal band of an apparently normal tissue, stained much brighter, by which it was separated from the adjacent lateral and anterior columns. The former exhibited a large area of degeneration (darkly stained in the photomicrographs); the latter were entirely normal.

Stained with toluidin blue, thionin, scarlet red, Van Gieson's or Bielschowsky's methods, the ventral horns showed a paucity of ganglion cells of which some, especially in the marginal band, were more or less well preserved. The majority, however, were decidedly pathologic (Fig. 3). Many were reduced in size and shrunken, their processes darkly stained and tortuous. Some cell bodies were distended and packed with pigment or lipoids. They were almost devoid of processes; their cytoplasm was homogeneous, sometimes without Nissl bodies,

Fig. 2.—Fifth cervical segment. The right (in the picture the left) ventral horn reduced in size. The marginal, healthy band, is well shown in the left (in the picture the right) cornu. Degeneration of the crossed pyramids is very marked (dark stained), the lateral limiting zone on the left (*L*) being comparatively well preserved. Alzheimer-Mann x 7.

which in some instances appeared dust-like or gathered at the periphery. Fibrils were few and were also displaced to the periphery where they formed a distinct layer, while the nucleus showed a folded membrane, was pale and usually dislocated towards the apical dendron which it almost invaded. In short the cells showed the phenomena of the so-called axonal reaction, central or total chromatolysis and sclerosis.

The marked degenerative cell changes were associated with pronounced proliferative neuroglial alterations. There were many so-called large cytoplasmic glia cells (Fig. 4) abundantly supplied with ramifying processes and a pale homogeneous cytoplasm containing a large eccentric nucleus rich in chromatin. So-called glia nuclei were exceedingly numerous, rich in chromatin and occasionally intermingled with fat granule bodies (gitter cells).

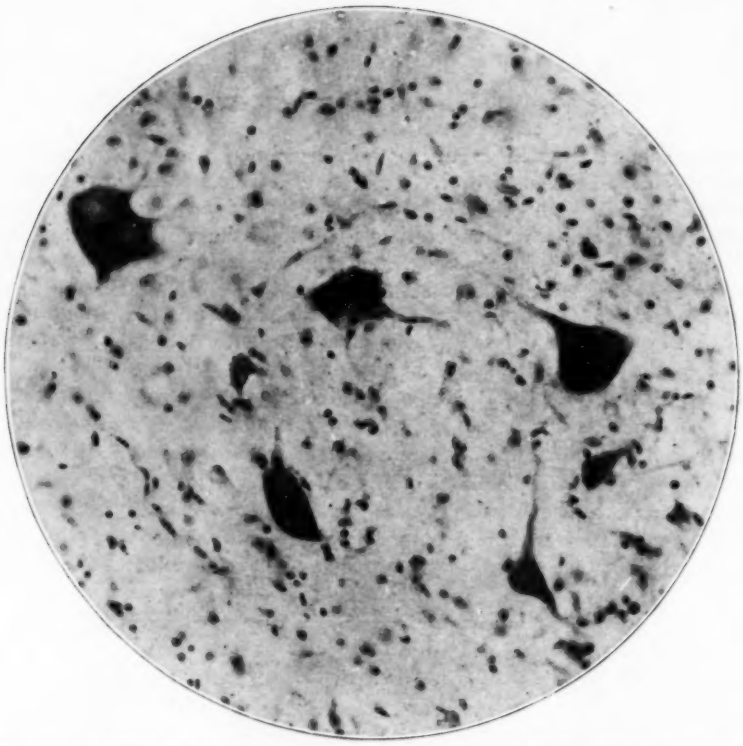

Fig. 3.—Ganglion cells from the comparatively healthy portions of the ventral horns. The changes are explained in the text. Toluidin blue x 230.

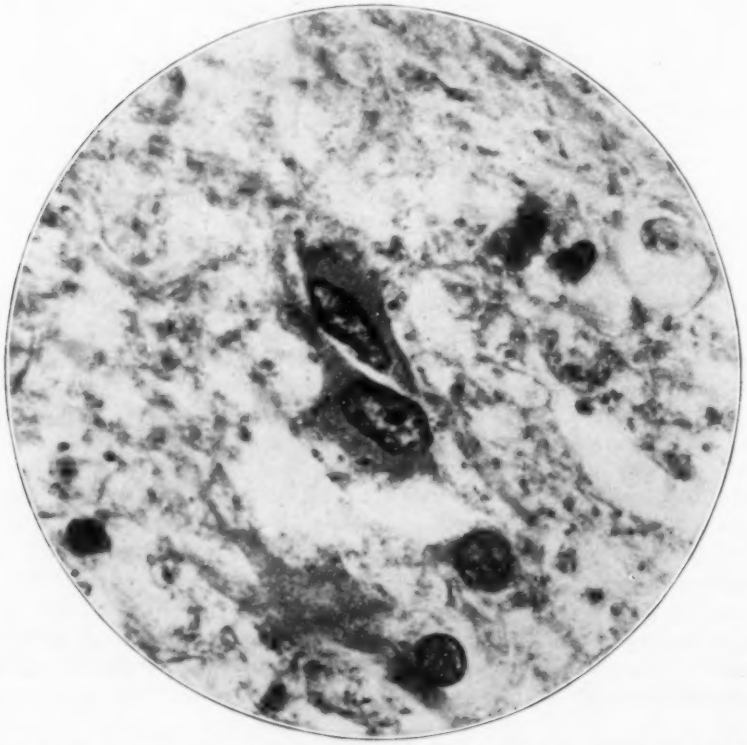

Fig. 4.—Large cytoplasmic glia cells in the ventral horns, outside the focus of softening. Alzheimer-Mann x 1200.

These regressive ganglion cell and proliferative neuroglial changes were present in both cervical and thoracic regions (the lumbosacral portion was not available for study). The thoracic were much less affected than the lower cervical segments (seventh and eighth) where distinct foci of degeneration or softening could be discerned (Figs. 5 and 6). They occupied the posterolateral area of the ventral horns, extended into the ventrolateral portion of the posterior horns, and consisted of a great mass of glia cells, principally fat granule bodies (gitter cells, Fig. 7), intermingled with cytoplasmic glia cells, glia nuclei and new formed capillaries. The foci thus formed were dense (Fig. 6) and were divided off from the neighboring, less damaged tissues by an excessive number of blood vessels

Fig. 5.—Focus of softening from the anterior horn showing as a triangle surrounded by rarefied tissue and vessels. Stain as in Figure 4 x 70.

(Fig. 5). The latter exhibited no inflammatory phenomena, such as lymphocytes, polyblasts or plasma cells, but their perivascular spaces were often distended and contained gitter cells or pigment. Ganglion cells were exceedingly sparse in the foci and for the most part in a state of advanced degeneration. They stained badly, were very small, much disfigured and shrunken; their processes were granular, tortuous and often surrounded and invaded by neurophages.

In contrast to these marked and widespread ventral horn changes, the posterior horns and Clarke's columns showed practically normal ganglion cells, though pathologic glia elements, such as cytoplasmic cell bodies, were occasionally present, especially in the neighborhood of the foci.

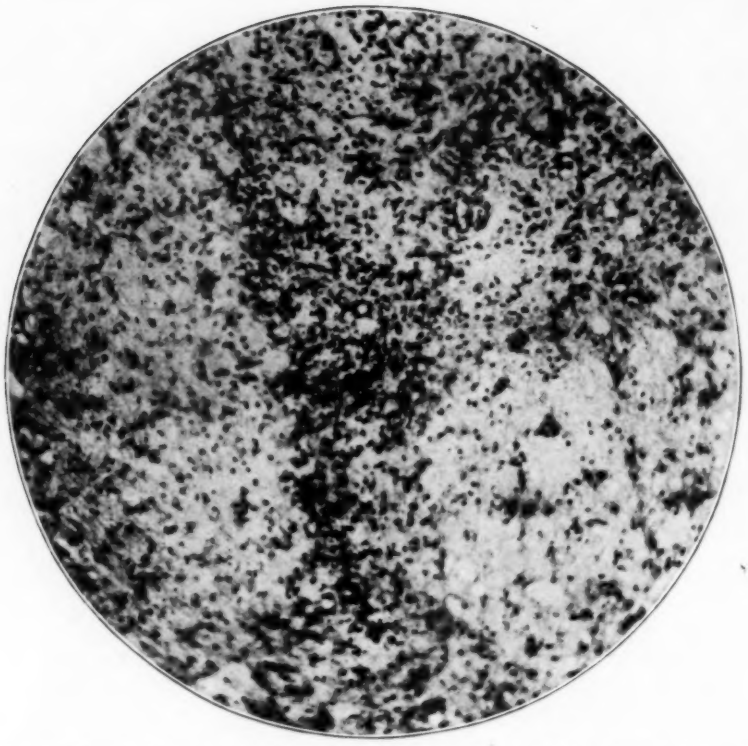

Fig. 6.—Same focus as in Figure 5, stained with toluidin blue x 110. Some of the cells are reproduced in Figure 7.

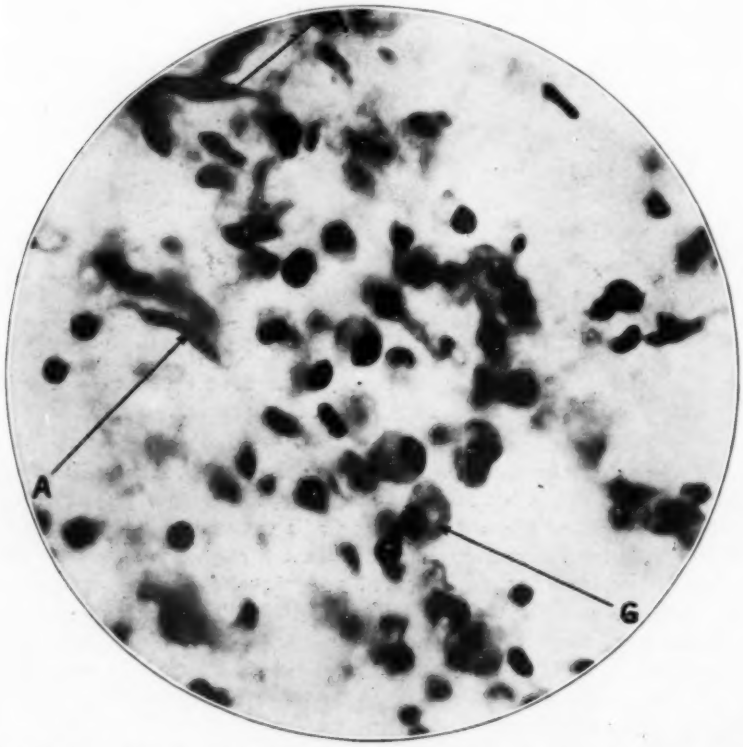

Fig. 7.—A higher magnification of some of the cells of the Figure 6. The majority are gitter-cells *G;* at *A* there are signs of new forming capillaries. Toluidin blue x 675.

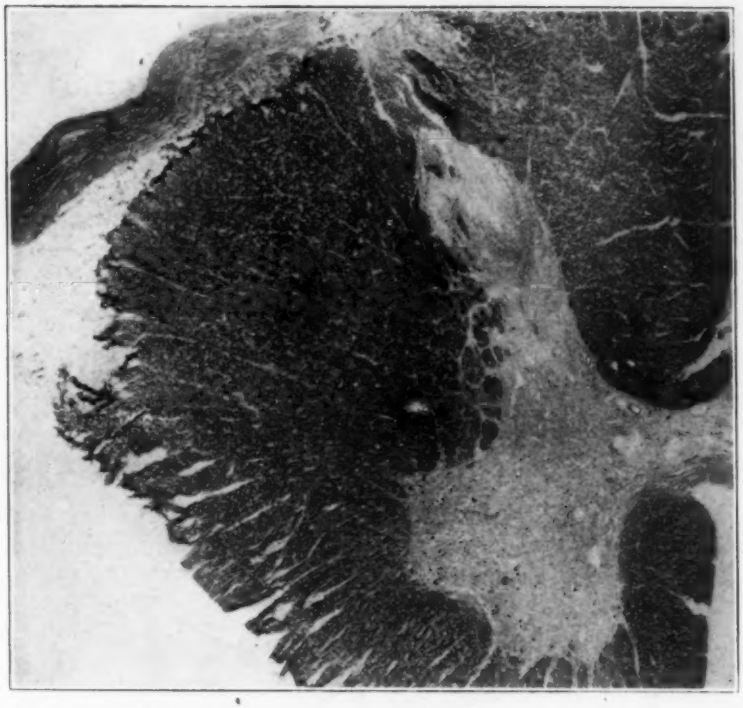

Fig. 8.—Seventh cervical segment. Degeneration of the crossed pyramidal tract encroaching on the lateral limiting zone. Paucity of cells in the ventral horn. Herxheimer's scarlet red x 15.

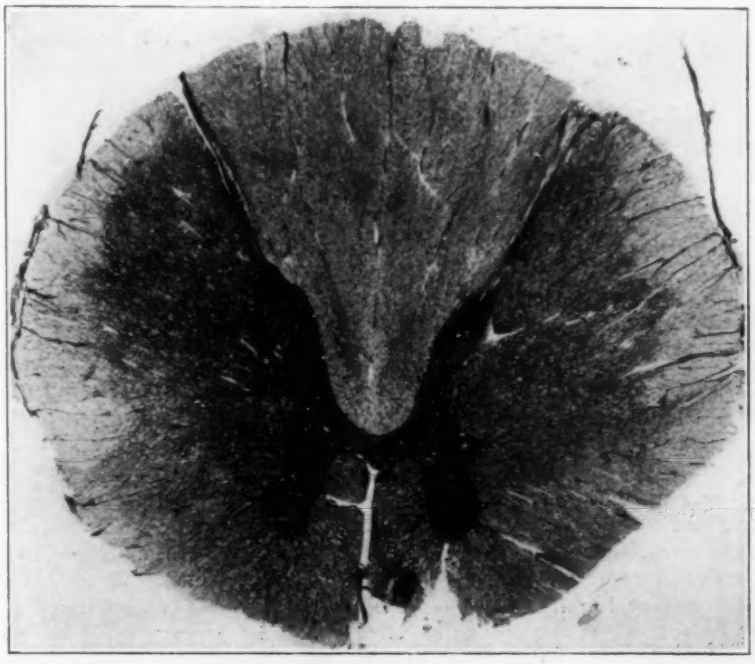

Fig. 9.—Fourth dorsal segment. Marked bilateral degeneration of the crossed pyramids, lateral limiting zones and Gowers' tract, especially on the right (in the picture on the left). The corresponding horn is smaller than the left (in the picture the right). Alzheimer-Mann x 10.

Equally pronounced were the changes in the lateral columns. As Figures 2, 8 and 9 show, there is an extensive degeneration involving the areas of the crossed pyramidal tracts, the lateral limiting zone and encroaching on the tract of Gowers; the rest of the white substance, including the anterior pyramids and the marginal portions of Gowers' tract, were entirely unaffected. Microscopic examination with the methods of Alzheimer-Mann, Bielschowsky, or these two staining methods combined, showed that in the degenerated areas, especially in the lateral limiting zone and the tract of Gowers, there were many normal fibers, the lateral limiting zone appearing sometimes, as in Figure 2, almost undamaged. In the thoracic segments, however, this area was markedly involved in both its ventral and dorsal limbs (Fig. 9), and in longitudinal sections (Fig. 10),

Fig. 10.—Longitudinal section of the lateral columns. The dark strands are axones, the lighter spaces between them are occupied by broken up myelin, axones and glia tissue: glia fibers, glia nuclei and other formations explained in text. Bielschowsky counterstained with Alzheimer-Mann stain x 285.

some fibers were found in a state of beginning or advanced secondary degeneration. The former was represented by broken up myelin, Marchi globules, abundance of cytoplasmic glia cells and myelophages; the latter—the advanced stage—by various types of fat-granule bodies. The myelin was slightly tumefied, the axones more or less irregular in shape and fragmented, but not swollen and without formation of the hyaline bodies described by Schmaus[5] and interpreted by Lhermitte[5] as fragments of greatly swollen axones.

5. Lhermitte, J.: Bull. et. mém. de la Soc. méd. d. hôp. **39**:680, 1915.

Stained with the methods of Marchi or Herxheimer, the crossed pyramidal fibers showed numerous black or red globules (Fig. 8) which were comparatively few, or even absent, in the lateral limiting zone and its adjacent areas. Here the process of nerve degeneration evidently was chiefly in the early stages. Blood vessels were rather sparse and often infiltrated with gitter cells, but, as in the gray matter, without signs of inflammation.

The anterior and posterior columns, the anterior commissure and the rest of the white matter showed no microscopic changes, regardless of the staining methods employed; nor did the anterior and posterior roots show any appreciable changes. The central canal was as a rule patent, surrounded by numerous ependymal cells, loosely scattered, hypertrophied and rich in chromatin. The pia-arachnoid was somewhat hyperplastic, containing many proliferated fibroblasts, mesothelial and a few gitter cells. The character of certain cellular elements could not be defined.

General Summary of the Pathologic Findings.—Widespread degeneration of the ventral horns with the formation of microscopic foci of softening, especially in the lower portion of the cervical enlargement of the spinal cord; secondary degeneration of some fibers of the crossed pyramidal tract, lateral limiting zone and the adjacent portion of Gowers' tract.

COMMENT

Resembling amyotrophic lateral sclerosis in the presence of a combined degeneration of the ventral horns and lateral columns, the case reported differs from it in the absence of degeneration of the anterior commissure and anterior pyramids; but more important, and in fact conclusive, is the presence of foci of softening. The latter were so minute that on superficial examination they escaped notice. Their presence in the ventral horns and the occurrence of large cytoplasmic glia cells and freely scattered gitter cells, are altogether foreign to amyotrophic lateral sclerosis. The microscopic picture of the lesions, however, closely resembled what Schmaus [3] described as "traumatic necrosis" in experimental concussion of the spinal cord.

By repeated blows against a board attached to the backs of guinea-pigs and rabbits vertically suspended in the air, Schmaus produced circumscribed foci of softening, cavities and systemic degeneration of the spinal cord. Especially marked in the areas which had been directly exposed to the blows, the foci were also scattered throughout the gray and white substances. The clinical symptoms were slowly progressive and lesions of the vertebral column and meninges were entirely absent. Schmaus ascribed the changes to "concussion," to direct injury to the spinal cord, which is actually destroyed; the changes are, therefore, demonstrable under the microscope. He apparently proved that the essence of spinal concussion is not a "molecular" change, an unfortunate and much misunderstood term introduced by Obersteiner [2] in 1879, but an actual histopathologic phenomenon. He also proved that, in its

genesis, contrary to assertions of Thorburn,[6] Gussenbauer [7] and especially Kocher, the vertebral column, the meninges and the blood vessels play no rôle whatever.

The findings of Schmaus have been confirmed by experimental studies of Bickeles,[8] Kirchgasser,[9] Fickler,[10] Jacob,[11] and Roussy, Lhermitte and Cornil,[12] as well as by numerous clinicopathologic studies by Hartmann,[13] Hellbach,[14] Finkelnburg,[15] Licen,[16] Redlich,[17] Jacob,[18] Claude and Lhermitte [19] and many others. Of especial interest are the cases in which the pathologic condition arose from shell explosions. In the cases of Lhermitte, and Claude, Lhermitte and Loyes [20] there was present so-called primary degeneration of the spinal cord fibers—excessive hypertrophy of the axones, swelling of the myelin, and the formation of myelophages with other neuroglial reactive phenomena.

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6. Thorburn, William: Cases of Injury to the Cervical Region of the Spinal Cord, Brain, **9**:510, 1887.

7. Gussenbauer, C.: Ueber Commotio Medullae Spinalis, Prag. med. Wchnschr. **18**: 485 and 496, 1893.

8. Bickeles, G: Zur path. Anat. der Hirn und Rückenmarks-erschütterung, Obersteiner's Arb. aus dem Neurol. Institut der Wiener Univ. **3**:102, 1895.

9. Kirchgasser, G.: Experimentelle Untersuchung über Rückenmarkserschütterung, Deutsch. Ztschr. f. Nervenh. **11**:406, 1897.

10. Fickler: Experimentale Untersuchungen zur Anatomie der traumatischen Degeneration und der Regeneration des Rückenmarks, Deutsch. Ztschr. f. Nervenh. **29**:1, 1905.

11. Jacob, A.: Experimentale Untersuchungen über die traumatischen Schädigungen des Zentralnervensystems (mit besonderer Berücksichtigung der Commotio Cerebri und Kommotionsneurose) Nissl-Alzheimer's Arb. **5**:182, 1912.

12. Roussy, G., Lhermitte, J., and Cornil, L.: Etude expérimentale des lésions commotionnelles de la moelle épinière, Ann. de méd. **8**:335, 1920.

13. Hartmann, F.: Klinische und pathologisch anatomische Untersuchungen über die complicierten traumatischen Rückenmarkserkrankungen, Jahrb. f. Psychiat. u. Neurol. **19**:380, 1900.

14. Hellbach, H.: Zur Kenntniss der Rückenmarkserkrankungen nach Trauma, Deutsch. Ztschr. f. Nervenh. **37**:321, 1909.

15. Finkelnburg, R.: Beiträge zur Klinik und Anatomie der Schussverletzungen des Rückenmarks, Deutsch. med. Wchnschr. **40**:2057, 1914.

16. Licen, E.: Beiträge zur Histopathologie der Schussverletzungen des Rückenmarks, Monatschr. f. Psychiat. u. Neurol. **42**:86, 1917.

17. Redlich, E.:: Ueber Rückenmarkserschütterung, Jahrb. f. Psychiat. u. Neurol. **38**:103, 1917.

18. Jacob. A.: Zur Pathologie der Rückenmarkserschüttering, Ztschr. f. d. g. Neurol. u. Psychiat. **51**:247, 1919.

19. Claude, H., and Lhermitte, J.: Etude clinique et anatomo-pathologique de la commotion médullaire directe par projectile de guerre, Ann. de méd. **2**:479, 1915.

20. Claude, H., Lhermitte, J., et Loyes, M.: Etude histologique d'un cas de commotion médullaire par éclatement d'obus, Bull. et mém. de la Soc. méd. d. hôp. de Paris **39**:680, 1915; Lhermitte. J.: Etude des lésions histologiques fines de la commotion de la moelle épinière, Ann. de méd. **4**:295, 1917.

In the case reported here, the white substance (the lateral columns) was involved, not in the form of a primary, but of a secondary degeneration, as described by A. Jacob [21] in his experimental studies. It also resembled the strictly degenerative changes that occur in the spinal cord, in conditions such as amyotrophic lateral sclerosis,[22] or similar degenerative states. The similarity to amyotrophic lateral sclerosis was enhanced by the fact that degeneration of the crossed pyramidal tracts was associated with that of the lateral limiting zone, a rather common occurrence in the former morbid condition. Holmes [23] frequently found also in the latter degeneration of Gowers tract and of the anterior pyramids. These last are involved with such remarkable constancy in descending degenerations following cerebral lesions, that their escape in my case would speak against a cerebral lesion, which is held responsible for the degeneration of the pyramidal tracts (crossed and direct) in amyotrophic lateral sclerosis.

It is most probable that the lesion of the crossed fibers in this case was secondary to that of the ventral horns, where so-called endogenous pyramidal fibers originate. The fact that the fibers suffered a more intensive and extensive lesion on the right side was presumably due to a more severe involvement of the right ventral horn. Marie [24] sees in the ventral horn lesions the cause of the degeneration of the pyramids in pellagra, and with Brissaud he [25] explains their degeneration in amyotrophic lateral sclerosis in a similar manner.

While this view may be extreme, there are other facts in favor of such an assumption. For instance Bing,[26] working in Edinger's laboratory on a case of acute anterior poliomyelitis of six weeks' duration, in which there was a marked and extensive destruction of the anterior gray matter only, found an appreciable number of degenerated fibers in both crossed and uncrossed pyramidal tracts. He named them "ground endopyramidal fibers" (fibrae endopyramidales propriae). The lateral endopyramidal fibers originate, according to Bing, in the ventrolateral portion of the posterior horns (in our case destroyed); the anterior endopyramidal fibers originate in the median marginal area of the

21. Jacob, A.: Ueber die feinere Histologie der sekundären Faserdegeneration, Nissl-Alzheimer's Arb. **5**:1, 1912.

22. Hassin, G. B.: Histopathologic Changes in a Case of Amyotrophic Lateral Sclerosis, Med. Rec. **91**:228 (Feb. 10) 1917.

23. Holmes, Gordon: Pathology of Amyotrophic Lateral Sclerosis, Rev. of Neurol. & Psychiat. **7**:693, 1909.

24. Marie, Pierre: De l'origine exogène ou endogène des lésions du cordon postérieur étudiées comparativement dans le tabes et dans la pellagre, Semaine méd. **14**:17, 1894.

25. Marie, Pierre: Sur la localisation des lésions médullaires dans la sclérose latérale amyotrophique, Semaine méd. **13**:533, 1893.

26. Bing, R.: Beitrag zur Kenntniss der endogenen Rückenmarksfasern beim Menschen, Arch. f. Psychiat. **39**:75, 1905.

ventral horns (in our case comparatively intact). The pyramidal fibers have been found degenerated also by Hellbach [14] in a case of spinal concussion that, clinically, very much resembled amyotrophic lateral sclerosis.

It is to be regretted that Roussy, Lhermitte and Cornil [12] do not mention the condition of the lateral columns in the dog in which they experimentally produced a concussion with a lesion of the anterior horns. As the animal survived the injury for six months the actual condition of the lateral columns would certainly have been of great interest.

The quoted instances are convincing demonstration that in my case the pyramidal degeneration probably depended on that of the ventral horns. It is much easier to understand the cause of the degeneration in the lateral limiting zone and the tract of Gowers. As these both originate in the ventral horns, they are more or less regularly involved in amyotrophic lateral sclerosis (Joffroy and Achard,[27] Bruce [28]) where the anterior limb only of the lateral limiting zone is affected (Bruce). In the case described, the involvement also of the posterior limb is probably due to the simultaneous lesion of the posterior horns (their basal portion) where, according to Bechterew, its fibers originate.

As noted, the lesion of the ventral horns was in the form of a slowly progressive degeneration of the ganglion cells. As such it was also described by Schmaus [3] and Jacob [11] in the experimental cases, and by Hartmann [13] Hellbach,[14] Westphal,[29] Jacob [18] and others in clinico-pathologic reports. The slow, though progressive, degeneration may account for the slow onset and the progressive course, since time is required for the corresponding nerves and muscles to become degenerated and produce symptoms that would force the victim to seek medical advice. In the case here recorded the interval between the injury and the appearance of the atrophy was about four weeks; it was the same in Hellbach's case. In Erb's case [30] it was but two weeks; in that of Duménil and Petel [31] six months; while in that of Goldberg,[32] the atrophy became marked about two years after the injury.

27. Joffroy, A., and Achard, Ch.: Note sur un cas de sclérose latérale amyotrophique, Arch. de méd. exp. et d'anat. pathol. **2**:434, 1890.

28. Bruce, Alexander: On a Special Tract in the Lateral Limiting Layer of the Spinal Cord, Scottish M. & S. J. **1**:41, 1897.

29. Westphal, A.: Ueber einen Fall von traumatischer Myelitis, Arch. f. Psychiat. **28**:554, 1896.

30. Erb, Wilhelm: Zur Lehre von den Unfallserkrankungen des Rückenmarks. Ueber Poliomyelitis anterior chronica nach Trauma, Deutsch. Ztschr. f. Nervenh. **1**:122, 1897.

31. Duménil, L., and Petel: Commotion de la moelle épinière, Arch. de neurol. **9**:1, 1885.

32. Goldberg, L.: Ein Fall von traumatischer amyotrophischen Lateralsclerose am untersten Theile des Rückenmarks, Berlin. klin. Wchnschr. **35**:263, 1898.

On the other hand, the onset, as well as the course, may be acute, especially in severe cases of concussion such as are caused, for instance, by shell explosions. Here both the gray and white substances are affected immediately after the injury, the resulting clinical symptoms—paralysis, anesthesia, bladder, trophic and similar disturbances—setting in early and acutely. In short, they may in their totality resemble the clinical picture of so-called contusion of the spinal cord, in which not only the nerve elements, but also the glia and the blood vessels are crushed outright by a fractured or dislocated vertebra or the resulting hemorrhage. However, in spite of the similarity in the clinical symptoms, there is great difference in the pathology as well as in the pathogenesis of these two conditions.

Pathogenesis of Spinal Concussion.—Much difference of opinion exists as to the mode of origin of the pathologic changes in concussion. Schmaus [3] explained them by disorders of lymph or spinal fluid circulation. The force producing the concussion is transmitted, he thinks, to the perivascular spaces and the central canal, the oscillations of the spinal fluid causing "tears" and "absorption" of the parenchyma. Gussenbauer and Lhermitte express somewhat similar views, while Henneberg [33] blames the blood vessels and the capillaries. He thinks that, because of concussion, the blood stops circulating and causes acute degeneration of the nerve elements and eventually their necrosis. Thorburn saw the cause in acute bending of the vertebral column, which at once "rights itself, but not before great or irreparable damage has been inflicted on the contained organ." Kocher considers every case of concussion as a contusion, the result of transient dislocations, fractures, etc., while Fickler sees the cause in "bruising" which the spinal cord undergoes when jarred, its fibers striking or pressing against each other or against the bony structures.

Without going into detailed discussion of the foregoing hypotheses I might point out that the essential cause of the pathologic changes is the concussion itself. A severe blow, a sudden stoppage of a fast moving train, an explosion of a shell or a fall, set the entire body in commotion, which is transmitted to the spinal cord. Here the most vulnerable and delicate elements, the ganglion cells, suffer most from the jar. In some of Jacob's experiments [11] they were the only elements that exhibited changes as described in this case. It is self-evident that concussion must occur in or be associated with contusion of the spinal cord, for if a force is powerful enough to cause a fracture or dislocation of a vertebra, it must also be strong enough to affect the soft semiliquid parenchyma, even far away from the region directly affected.

33. Henneberg: Erweichung des Sacralmarkes nach Schuss in die Brustwirbelsäule, Berlin. klin. Wchnschr. **52**:859, 1915.

In other words concussion is a very common occurrence in contusion. In Obersteiner's [2] patient, a bullet lodged in the arches of the cervical vertebrae caused a large focus of softening in the lumbar region of the spinal cord. In Licen's case,[16] a fracture of the third, fourth and fifth lumbar vertebrae was combined with a necrosis of the sacral region of the cord. In the patient of Henneberg an injury to the eighth thoracic vertebra caused a sacral cord lesion; in Kocher's case dislocation and fracture of the tenth and eleventh vertebrae was associated with necrosis of the lumbosacral region; and Hellbach describes degenerative foci throughout the spinal cord after an injury to the neck. Widespread, scattered foci of softening may well account for some of the strange and paradoxical clinical phenomena, such as flaccid paraplegia with loss of tendon reflexes, observed in traumatic and other transverse lesions of higher spinal segments. In quite rare traumatic cases, in which flaccid paralysis was absent, scattered foci of softening evidently were lacking. Thus complete sections of the spinal cord produced by surgeons or in experiments on animals, or transverse lesions secondary to pressure by tumors—in short, strictly localized or focal destruction of the spinal cord—will not cause the phenomena known as Bastian's law.

Affecting in its pure (uncomplicated by a contusion) form any level of the spinal cord, its white or gray substance or both, a concussion must necessarily produce a great variety of clinical syndromes. These may be as typical as when caused by an infectious or a degenerative process, and may even resemble, as in this case, the clinical picture of amyotrophic lateral sclerosis. As compared with the rather numerous cases of so-called traumatic myelitis, syringomyelia, hematomyelia, multiple sclerosis and various myopathies, a clinical picture of amyotrophic lateral sclerosis following trauma is altogether rare. Mott,[34] Kienböck,[35] Goldberg,[32] Seiffer,[36] Giese,[37] Sarbo [38] and especially Erb [39] reported clinical instances of post-traumatic muscular atrophies, some of which (the cases of Goldberg, Seiffer and Giese) were those of a typical amyotrophic lateral sclerosis. Still fewer of this sort were studied patho-

34. Mott, Frederick: Concussion of the Spine from a Fall Followed by Wasting and Paralysis of Numerous Muscles in Both Arms, Glossy Skin and Loss of Sensation of Right Arm, Brain **10**:478, 1888.

35. Kienböck, R.: Atrophy Following Trauma, Wien. med. Presse, **40**:1926, 1899.

36. Seiffer, W.: Ueber organische Nervenkrankheiten nach Unfällen, Charité Ann. **27**:542, 1902.

37. Giese, O.: Amyotrophische Lateralsclerose nach Trauma, Deutsch. med. Wchnschr. **30**:1348, 1904.

38. Sarbó, A.: Klinisch reiner Fall von spastischer Spinal-paralyse (Erb) als Unfallfolge, Deutsch. Ztschr. f. Nervenh. **46**:43, 1913.

39. Erb, W.: Zur Lehre von den Unfallserkrankungen des Rückenmarks, anschliessend an einen Fall von progressive spinaler Amyotrophie durch Ueberanstrengung, Deutsch. Ztschr. f. Nervenh. **45**:1, 1912; ibid. **38**:261, 1910; see also reference in Footnote 30.

logically. Here belong the cases of Duménil and Petel,[31] Joffroy and Achard,[27] Hellbach,[14] Astwazaturow [40] and an old case of Maty (1776) quoted by Erichsen.[41]

In conclusion I might call attention to the fact that multiple foci of softening, as described in the case reported here, may also be present in the brain. Such a case has been reported by Bassoe and me.[42] Whether the etiology—concussion—was also responsible in that case for the multiple disseminated foci of degeneration I am unable to tell. Such an etiology, however, should be borne in mind in cases of cerebral and spinal cord lesions in which the history is obscure, the onset atypical and the course unusual.

The medicolegal importance of cerebrospinal traumatic lesions due to concussion is obvious and needs no discussion.

CONCLUSIONS

1. Concussion of the spinal cord produces definite histopathologic lesions in the form of foci of softening, which do not depend on the condition of the vertebral column, meninges or vessels.

2. The foci may be so minute as to escape notice on superficial examination.

3. They may be confined to the gray matter.

4. In case the ventral horns are principally affected, they may give a clinical picture of amyotrophic lateral sclerosis.

5. The onset of the clinical symptoms may be slow and the course progressive, depending on the time necessary for the nerve degeneration to become manifest.

DISCUSSION

DR. PETER BASSOE: I would like to say something about this case because it is an extremely interesting and, I think, a very important one. I first saw this man March 29, 1922. Remember that the whole course of this case was only sixteen months. Nov. 3, 1920, he fell on his right shoulder and, turning over, he felt a cramp in the right arm for a few minutes and a pain in the neck. He went back to work. On Thanksgiving day, three or four weeks later, he noticed some weakness in the right hand, and this weakness, as Dr. Hassin said, extended to the other hand and arm. In August, 1921, he was still able to raise the arm. When he came to the County Hospital in October, the weakness had progressed and it continued to progress. At the time I saw him, both arms hung down in a perfectly flaccid state, but he could jerk his shoulders. There was no movement of the other shoulder muscles; no power in the left biceps and only slight power in the right one. He had some power in the wrist and fingers. The atrophy was most marked, as I remember, in the upper part of the arms.

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40. Astwazaturow, M.: Ein Fall von post-traumatischer spinaler Amyotrophie nebst Bemerkungen über sogenannte Poliomyelitis anterior chronica, Deutsch. Ztschr. f. Nervenh. **42**:352, 1911.

41. Erichsen, J. E.: On Concussion of the Spine, New York: William Wood & Co., 1883, p. 5.

42. Hassin, G. B., and Bassoe, Peter: Multiple Softening Versus Multiple Sclerosis, Arch. Neurol. & Psychiat. **7**:613 (May) 1922.

Breathing was almost wholly thoracic. The tendon reflexes of the arm were absent; the knee and ankle reflexes were increased; there was no Babinski sign. The abdominal reflexes were entirely absent, so there was some evidence of pyramidal tract involvement that, I should think, would include more than the endogenous fibers. In view of the history and the suspicious roentgen-ray appearance, I thought laminectomy would be justified, especially as I knew that such an operation by Dr. Roberg would not be a very serious risk. Everything went very nicely until the terminal illness appeared.

When it comes to placing this case, I wish to remind you of the history of anterior poliomyelitis. When its pathology was written, chiefly by Charcot and his co-workers, it was based entirely on old cases with shrunken cells and cord; not a word was said about the acute inflammatory phenomena. That was all worked out afterward when fatal cases were examined during epidemics. The question to me is, after all, was not this a case of amyotrophic lateral sclerosis? The histologic picture of that disease which we have in mind is based chiefly on the examination of cases that died years after the onset. I would like to ask Dr. Hassin if there is not the possibility that, in the early stages, there may be involvement beyond the pyramidal zone. Then, furthermore, in a traumatic case one would expect the initial symptoms to be more severe. Here they were almost nothing. The disease began three or four weeks after the injury, which certainly was not severe, but there was steady progression and it continued to the end, through a period of sixteen months. There were no bulbar symptoms, so the course was interrupted before it had reached the stage at which we are accustomed to see the cord postmortem.

Dr. Lewis J. Pollock: I cannot add anything from a clinical standpoint except to state that it impressed me as a case of amyotrophic lateral sclerosis. I think, too, it should be said that there was definite weakness in the legs and certainly increased tonus. The man had spastic paraparesis without sensory changes. The cases of necrosis of the cord following concussion which were observed in the war, and there were quite a number, some having been reported by Madame Benisty, followed such a course as one might suppose would occur. They, too, did not develop immediately after the injury but usually from one to two weeks later. Men who had had through and through gunshot wounds of the neck, without the spine having been touched, would exhibit a brachial plexus lesion with atrophy, flaccidity and paresis of the arm, and later would develop a typical Brown-Sequard paralysis. In other words, the necrotic areas did not seem to be limited to any particular system and were of sufficient extent to produce an ordinary unilateral transverse lesion of the cord. I would like to know whether it is common in anterior poliomyelitis to find so large an involvement of the lateral tract, endogenous or not, which would give rise to such a marked increase in reflexes and weakness in the lower extremities. Certainly, in pellagra, the changes in the anterior horn cells, and particularly in Clark's column, are definiely axonal and are secondary to the changes in the lateral columns, not at all as would seem to be the condition in this case.

I might add that the cases Benisty observed usually died a number of weeks after their onset.

Dr. Hugh T. Patrick: It is dangerous to discuss a case one has not seen and to express an opinion of slides which one has not examined, but I must confess that Dr. Hassin's presentation is very unconvincing to me. If involvement of the anterior horn cells causes such extensive change in the lateral tract as that in Dr. Hassin's case, why do we not see it in the thousands of cases of anterior poliomyelitis? Again, why should concussion cause steadily progressing degeneration?

Another very important bearing of this case is its medicolegal aspect. If we are to believe that such a trifling concussion as this patient received is to give rise to such extensive progressive involvement, any person with amyotrophic lateral sclerosis may recall some past trivial injury and claim compensation. I understand this patient was compensated for injury. I think it would not be either safe or proper from the clinical, pathologic or medicolegal aspects to accept this case without criticism.

Dr. H. Douglas Singer: I would like to ask Dr. Hassin if the areas of softening are absolutely limited to the anterior horns, or whether he finds similar foci in other regions. There are a number of other degenerations shown in these sections which would be very difficult to explain on the basis of the anterior horn lesions. As has already been emphasized by others, it is difficult for me to understand the sequence of events. A traumatic lesion should surely be worse at the time of the trauma and further progress should be in the direction of improvement.

In the cases mentioned by Dr. Pollock, is it not possible that the progressive lesions were caused by toxic action from an infected wound?

Dr. Pollock: I cannot state, as I do not recall the condition of the wounds at this time. The cases I saw of through and through wounds of the neck were very rarely associated with infection.

Dr. G. B. Hassin: It will take too much time to answer in detail all the questions asked. The various problems pertaining to the histopathology of this case are more or less fully covered in my paper, which I hope will convince Dr. Patrick that this is not a case of amyotrophic lateral sclerosis. Clinically it may appear such, but pathologically it is decidedly not. The photomicrographs show clearly the presence, in the ventral horns, of cytoplasmic glia, gitter cells and foci of softening or necrosis, which is altogether foreign to amyotrophic lateral sclerosis and is rather typical of concussion of the spinal cord.

Dr. Patrick is perfectly right in saying that if the pyramidal tract degeneration in this case is secondary to the ventral horn lesion, it should also be present in anterior poliomyelitis. Bing, in 1905, working in Edinger's laboratory on a case of anterior poliomyelitis, did demonstrate involvement of the pyramidal tracts and he introduced the term "ground endopyramidal fibers."

As to the pyramidal tract lesions in pellagra, I do not know its exact nature. It has not been studied. Even Singer and Pollock in their careful histopathologic study of changes in the central nervous system in pellagra do not describe the histologic changes in the pyramidal fibers.

The changes in Gowers' tract and the lateral limiting zone are certainly secondary to the lesion of the ventral horn cells. Many of the latter showed the axonal reaction in progressive muscular atrophy described by Alzheimer in 1892 and as occurring in spinal concussion by Hellbach. The ventral horn ganglion cell changes evidently are the primary pathologic phenomena; those of the pyramidal fibers, Gowers' tract and lateral limiting zone are secondary. As time is required for a nerve fiber to become degenerated and produce manifest clinical symptoms, it is easy to understand the gradual onset and progressive course. The latter thus speaks rather for than against the diagnosis of concussion.

I must admit that this was a difficult and baffling case which, at the beginning of my studies, strongly appealed as one of amyotrophic lateral sclerosis. An enormous number of sections, studied with many staining methods, enabled me to find changes which convinced me that this is not a case of amyotrophic lateral sclerosis.

SPONTANEOUS CEREBRAL LESIONS IN MONKEYS

THEIR SIGNIFICANCE IN EXPERIMENTAL PATHOLOGY *

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In the experimental investigation of certain diseases of the nervous system occurring in human beings, primates have been the favorite laboratory animals, for their close phylogenetic relationship to man and the morphologic similarity of their tissues render the interpretations of the induced lesions clearer and make deductions drawn therefrom more probable. A study of the neuropathologic anatomy of monkeys and apes seemed therefore of interest, not only to the comparative pathologist, but also to the experimental neurologist; for a knowledge of the spontaneous lesions that may occur in such animals may prevent misinterpretation of changes found after an experiment. Through the kindness of Dr. Herbert Fox, the director of the Laboratory of Comparative Zoology of the Philadelphia Zoological Garden, a number of brains from primates which had died at the garden were made available. The organs were hardened in formaldehyd and sections taken routinely from various portions of the cortex, pons, and in many instances from the basal ganglions. Both celloidin and paraffin sections were made and these were stained with cresyl-violet, toluidin-blue, hematoxylin and eosin, and, after zenkerization, with Mallory's phosphotungstic acid-hematoxylin.

Changes of some type were practically always found in the ganglion cells, but since these could often be interpreted as the result of the terminal disease, or even as postmorten degenerations, they will be referred to only in as far as they accompany more defined structural alterations. In order to avoid repetition, a list of the animals with their anatomic diagnoses is appended.

The types of lesions may be grouped under the following heads:

NONSUPPURATIVE MENINGO-ENCEPHALITIS

Two animals, both baboons, presented lesions indistinguishable from those found in human acute poliomyelitis and epidemic encephalitis, as shown in the detailed protocols given below. The meninges were infil-

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* Investigation aided by a grant from the Research Institute for Cutaneous Medicine, Philadelphia.

trated here and there with round cells. Many of the smaller vessels, particularly those in the pons, possessed jackets of several layers of lymphocytes and plasma cells. These cells were usually strictly confined to the adventitial sheaths, but occasionally they extended beyond the limiting glial membrane, and occurred as irregular scattered foci in the cerebral substance. There was a mild proliferation of the cellular glia. Various ganglion cell changes were present, but, as has already been stated, it is difficult to evaluate these. The clinical notes of these two animals are meager. The Chacoma baboon, whose habitat is in South Africa, was received in apparently good health, but became ill a

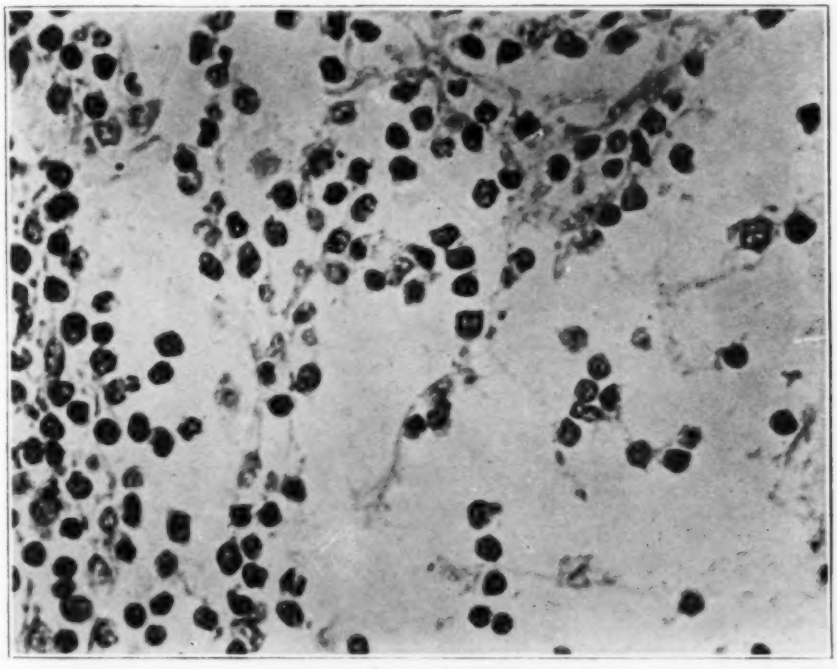

Fig. 1.—Yellow baboon (Papio cynocephalus), Animal 1. Sulcus from parietal region. The pial meshes are infiltrated with mononuclear cells, most of which are lymphocytes. A few plasma cells and many intermediate forms are present. The occasional elongated, pale, oval nuclei belong to fibroblasts.

few days after arrival. The yellow baboon, whose habitat is in western and central Africa, lived in the gardens for five years. It was noted that he became weak in the hind quarters about one year before death, but since osteomalacia was found in the thoracic and pelvic bones the weakness was probably not cerebral in origin.

A third animal, a still-born rhesus monkey, had brain changes which are very difficult to interpret. The meninges were normal. There was perivascular, as well as focal, infiltration of lymphocytes and plasma cells

in the basal ganglions and a very prominent proliferation of the cellular glia. The capillary endothelium was swollen, and vascular budding was frequently found. It is possible that the lesions were due to an infection contracted during intra-uterine life. Clinical notes were not available.

Animal 1.—Yellow baboon (*Papio cynocephalus*) P. Z. G., 4244. The leptomeninges, over the entire brain, were moderately edematous; the vessels were well engorged. Irregularly distributed round cell infiltration was present in moderate degree, but was particularly marked in the pial prolongation into the cerebral sulci. The adventitial lymph spaces were sometimes mildly infiltrated, but, as a rule, the various cellular elements were distributed through the pial

Fig. 2.—Yellow baboon (Papio cynocephalus), Animal 1. Pons: three small vessels with marked perivascular round cell infiltration. The majority of the pontile vessels possess similar mantles.

meshes, without relation to the bloodvessels. A few large, oval, pale, vesicular nuclei with more or less abundant spindle-shaped or oval cell body, denote early connective tissue proliferation; there was, however, no increase of collagenous fibrils. The adventitial cells were frequently swollen and appeared to be proliferating slightly. The vascular endothelium was somewhat prominent; budding was not present. (Fig. 1). Several types of infiltrative cells occurred, the majority being typical lymphocytes with small cytoplasmic rim, richly chromatic nucleus, and usually well marked nucleolus. There were also typical plasma cells with large, oval or polygonal, somewhat basophilic cell body, and an eccentrically placed, reticulated nucleus, surrounded by a clear "court."

There were many intermediate forms, indeed, these sometimes predominated: large lymphocytes with less regularly rounded nucleus, small plasma cells, and other mononuclear elements difficult to group. Degenerative forms were frequently seen; they possessed a puffed, vacuolated or finely reticulated cell body, and a shrunken hyperchromatic nucleus. Polymorphonuclear leukocytes and fibrin were absent. In the pons, the cell infiltration was most marked and all parts appeared equally involved. Here, in nearly all of the smaller vessels, and in several of the larger veins and arteries, the adventitial sheaths (Virchow-Robin spaces) were more or less thickly infiltrated with lymphocytes, occasional plasma cells and intermediate forms. (Figs. 2 and 3). This infiltration was usually strictly confined to the adventitial sheaths, and only very occasionally extended beyond the membrana limitans gliae. In a few places there were

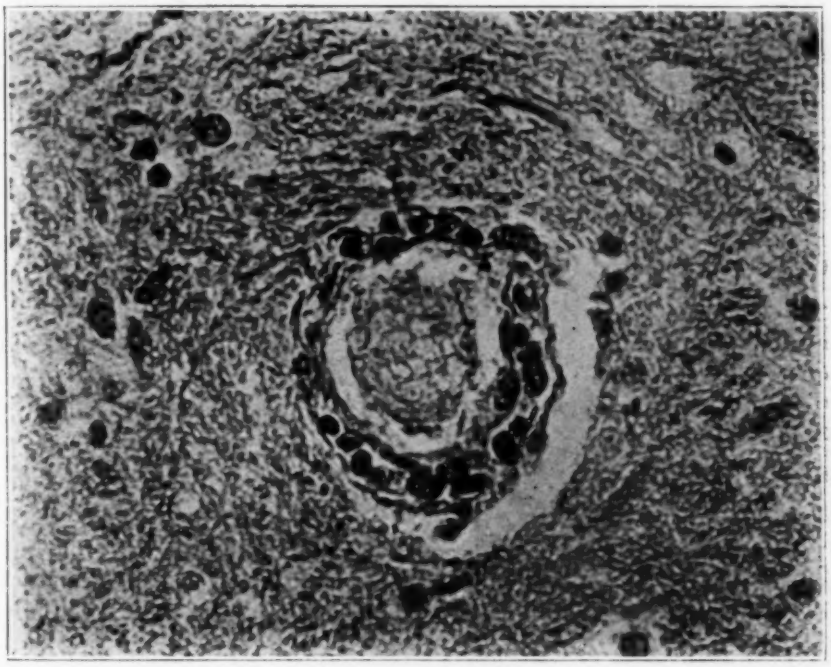

Fig. 3.—Yellow baboon (Papio cynocephalus), Animal 1. Pons: a higher power photomicrograph of a small venule with a lymphocytic exudate in its adventitial sheath.

small, irregular infiltrative foci, apparently not related to blood vessels. All these cells conformed to the types found in the meninges; a small number presented retrogressive changes.

In the cerebral and cerebellar cortex, in the white matter and the basal ganglions, perivascular and focal infiltrations were found only occasionally. There was no distinct engorgement, and hemorrhages were nowhere encountered. The capillary endothelium was mildly swollen, but vascular budding, or newly formed capillaries were not present.

The glia was not much affected, only the subependymal layers were somewhat proliferated. The ganglion cells often possessed swollen, vacuolated cell

bodies, their chromatin granules were obscure, and their nuclei were frequently eccentrically placed. But this was too uniformly present to be an antemortem process, and probably should be regarded merely as postmortem degeneration. Neuronophagy was not found. A few ganglion cells possessed two nuclei, a condition not infrequently seen in animals.

Animal 2.—Chacma baboon (*Papio porcarius*) P. Z. G., 5060. The leptomeninges were here and there slightly thickened and infiltrated with small numbers of lymphocytes, and very occasional plasma cells. The connective tissue was proliferating; there were numerous fibroblasts, as well as an increase of collagenous fibrils. The most marked lesions were present in the pons, where almost all of the vessels were enveloped by a mantle, several

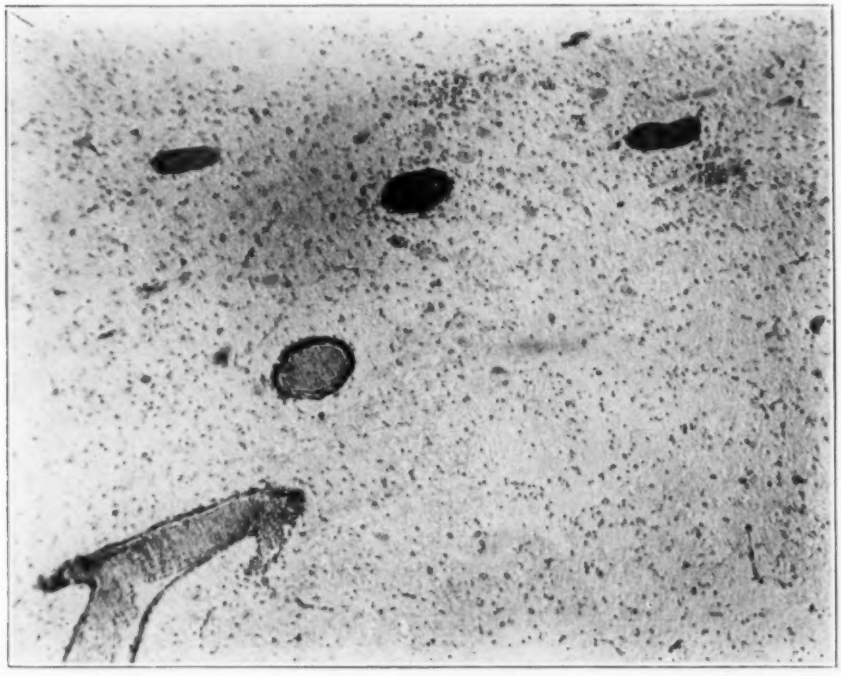

Fig. 4.—Chacma baboon (Papio porcarius), Animal 2. Pons: marked adventitial small round cell infiltration. In the upper portion of the photograph there are two small cellular foci unrelated to blood vessels. Similar lesions are frequently found.

cells deep, of small round cells (Figs. 4 and 5). These, typically, were confined to the adventitial spaces and were mainly lymphocytes, larger forms which probably represented intermediate stages between lymphocytes and plasma cells, and rare typical plasma cells. There were a number of cellular foci unrelated to the blood vessels; their component elements appeared to be chiefly proliferated neuroglia cells; they had pale, frequently irregular nuclei and often indistinct, irregular cell bodies. Intermingled with them were lymphocytic elements indistinguishable from those found in the adventitial sheaths, and a number of very large and pale vacuolated nuclei, possibly belonging to degenerating lymphocytic or neuroglia cells. Typical plasma cells

were not found. The impression was gained that the perivascular exudation constituted a different process from the focal infiltration. In the basal ganglions, and very occasionally in the white matter of the cerebellum, there were a few similar lesions.

Many of the arteries, particularly those in the basal ganglions, had irregularly thickened, partly hyalinized, and often calcified walls; this condition was present even in some of the smallest arterioles.

The neuroglia, especially in the pons, had slightly proliferated but, curiously, no overgrowth of the subependymal layers was present. The most marked changes occurred in the region of the cellular infiltrations; here granular and vacuolated or reticulated glia cells were often found.

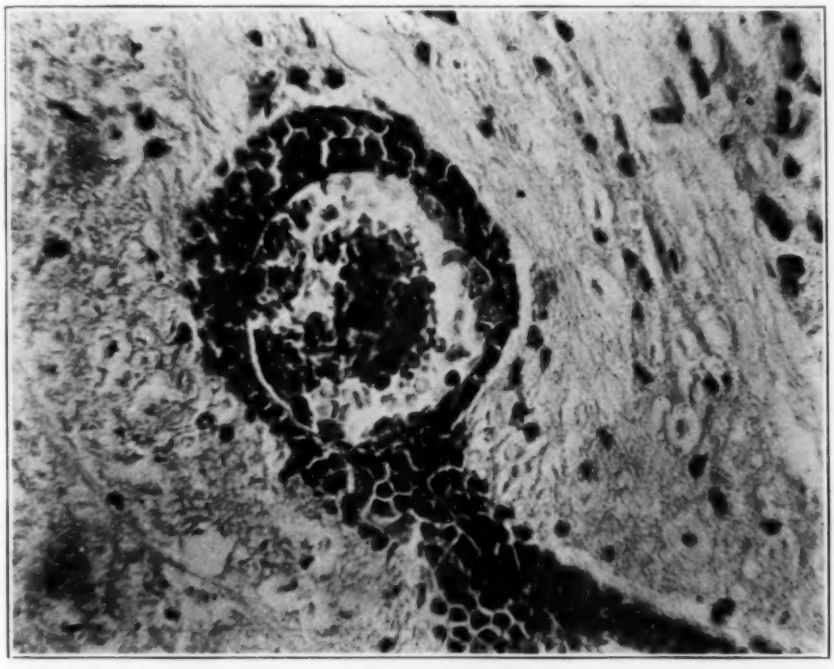

Fig. 5.—Chacma baboon (Papio porcarius), Animal 2. Pons: higher power photomicrograph of a small venule with a lymphocytic exudate in the adventitial sheath. The infiltrating cells are not confined to the vessel but extend beyond its boundaries.

The nerve cells exhibited chronic, as well as acute degenerative alterations. They were frequently shrunken, their processes were distinct and tortuous, their nuclei small and compact. Hugely swollen vacuolated elements, cells with pale or achromatic nuclei and with fragmented cell bodies occurred. A small number of elongated sausage-shaped nuclei with delicate, almost fibrillar, cell bodies were seen in different cortical regions. They corresponded to rod (Stäbchen) cells. Occasionally the neuroglia cells around the degenerated ganglion cells were increased in numbers; they sometimes lay within the place previously occupied by degenerated portions of nerve cells, or even within their

bodies. Polymorphonuclear elements were absent. There was no vascular engorgement, nor any swelling of the capillary endothelium. Formation of new vessels was nowhere seen.

Animal 3.—Stillborn rhesus (*Rhesus macacus*), 189. The pia-arachnoid was normal. In the basal ganglions and the internal capsule the vessels were greatly engorged. Similar, but less uniform, hyperemia was found in some portions of the cortex and the medulla. The pons contained a few focal hemorrhages. The vessels, in general, possessed a slightly swollen endothelium, which became pronounced in the capillaries and the small venules and arterioles of the basal ganglions and the internal capsule. Here frequent "budding" was

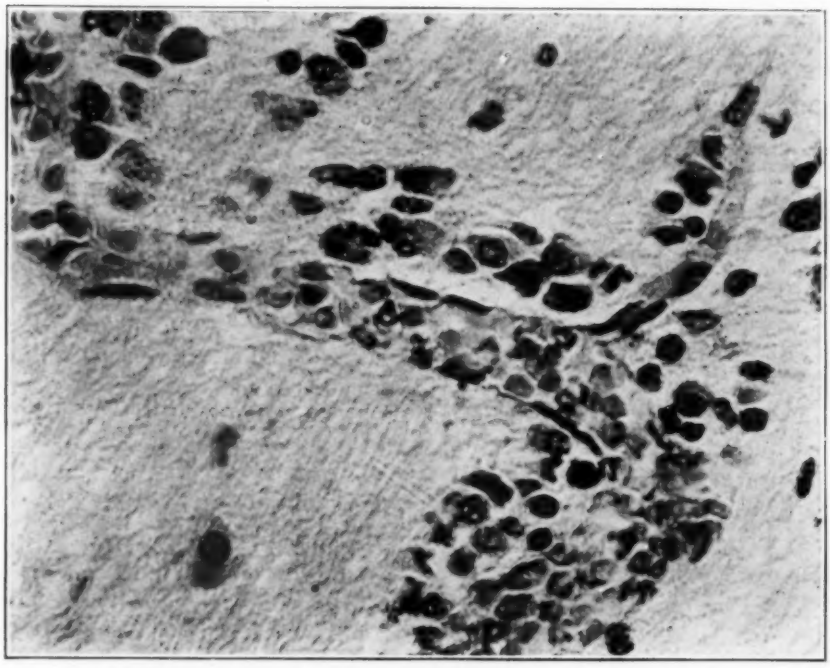

Fig. 6.—Still-born rhesus monkey, Animal 3. Internal capsule near lateral ventricle. A longitudinal section of a prevenule. The endothelium is slightly swollen. On the upper right is a small tapering branch with greatly swollen endothelium, the uppermost cell of which is particularly hyperplastic. Bordering the vessel, but not infiltrating it there are collections of large, richly protoplasmic, round, oval or polygonal mononuclear cells, many of which bear resemblance to plasma cells in that they possess an eccentrically placed nucleus, with a richly chromatic nuclear wall and chromatic clumps scattered through the pale nuclear body. Some possess a pale perinuclear "court." The protoplasm is usually smooth, but sometimes clumpy or granular; infrequently it has basophilic tendencies. Similar cells lie at a distance from the vessel. All these are probably very youthful protoplasmic glia cells.

encountered. The smaller vessels in the immediate neighborhood of the lateral ventricles were often surrounded by chains and irregular groups of large mononuclear cells, oval, round or polygonal in shape, with fairly sharply

delineated cytoplasm. This was usually smooth, but sometimes clumpy, vacuolated or reticular; sometimes it exhibited basophilic tendencies, but as a rule it was mildly acidophilic. The nuclei were commonly eccentrically placed, and possessed a well marked membrane bordered by small irregular clumps of chromatin; a few such clumps were scattered through the pale interior. An occasional cell exhibited a clear perinuclear court. In short, many of these cells closely resembled plasma cells. The majority, however, probably were youthful protoplasmic glia cells, for similar elements were scattered throughout the nervous parenchyma. They showed various proliferative and degenerative forms. Granule (Körnchen) cells, and reticulated (Gitter)

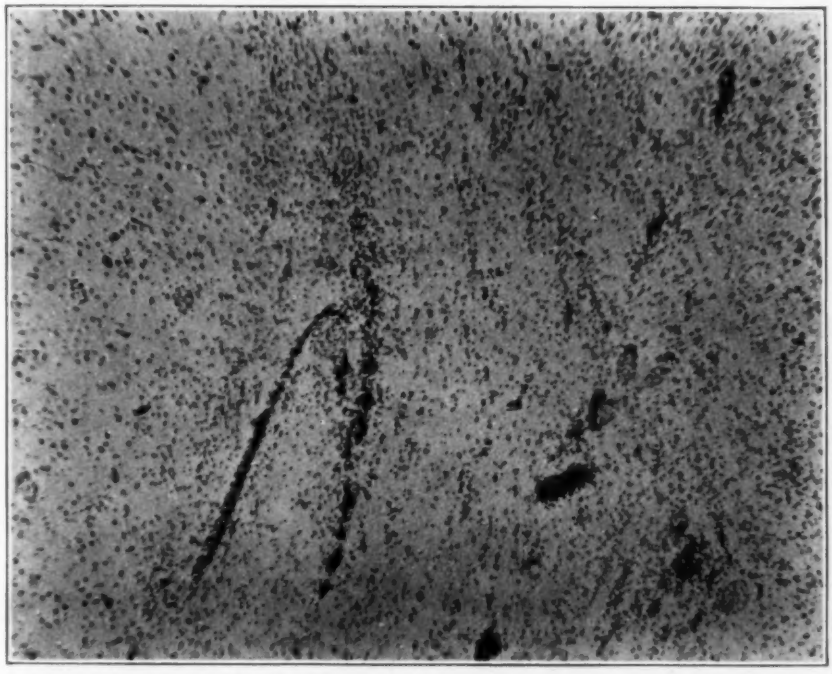

Fig. 7.—Still-born rhesus monkey, Animal 3. Head of caudate nucleus. Perivascular and focal small round cell infiltration; increase of neuroglia cells.

cells in moderate numbers were often seen. Frequently there were epithelial-like rows of protoplasmic glia cells adjoining capillaries. Pictures such as these, are confusing and no doubt have often been grouped under "perivascular small round cell infiltration" (Fig. 6), particularly when such infiltration was coexistent. In this monkey extensive lesions were located chiefly in the basal ganglions and especially in the head of the caudate nucleus. Here the smaller vessels, particularly the venules, were surrounded by a mantle several layers in thickness of lymphocytes with moderate numbers of plasma cells (Fig. 7). The infiltration was not everywhere limited to the perivascular sheath but here and there involved the nervous parenchyma (Fig. 8). The neuroglia cells were increased in numbers and appeared to be actively proliferating, many very large irregularly shaped protoplasmic elements being present. The subependymal glia, in particular, was hyperplastic and had pushed the ependyma

forward (ependymal granulation). Rod cells, both in close relation to the vascular adventitia and free, were often encountered. Polynuclear leukocytes were absent. The nerve cells exhibited some degenerative changes, but the swelling and chromatolysis present were probably expressions of postmortem alteration. Neuronophagy was not observed.

ARTERIOSCLEROSIS

Under this heading are included all chronic arterial lesions. Four animals showed more or less well-marked cerebral arteriosclerosis. The most important is the pigtailed macaque, for definite statements as to

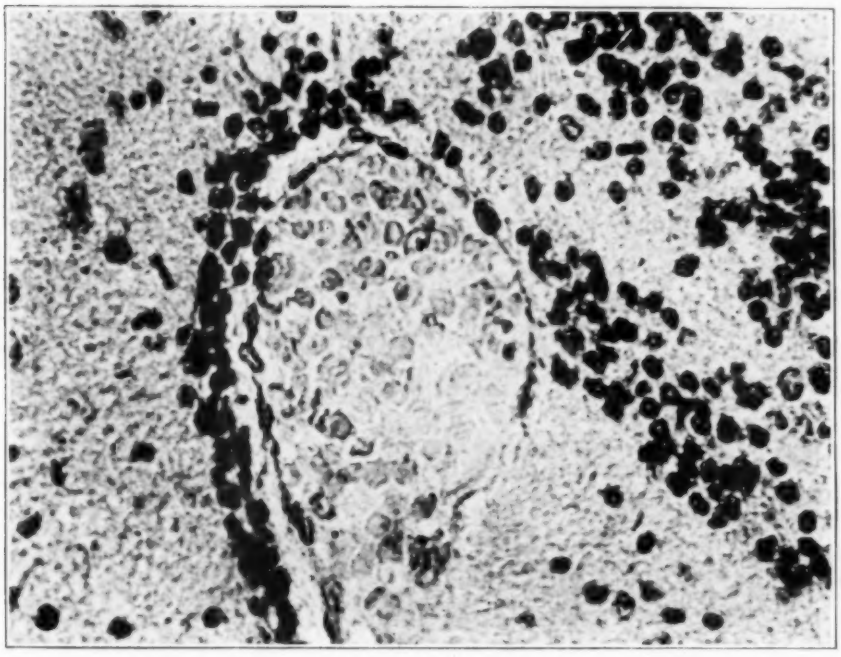

Fig. 8.—Still-born rhesus monkey, Animal 3. Head of caudate nucleus. Higher power photomicrograph of venules to left of center of Fig. 7. The adventitial sheath of the venules is infiltrated with several layers of lymphocytes and occasional plasma cells. On the right side of the figure an irregular focus of similar cells is shown; here the plasma cells are more in evidence.

the age of this animal are available. It was born in the garden Aug. 18, 1918, and found dead June 3, 1919; it was, therefore, less than a year old. Its vessels were markedly sclerotic and atheromatous, and generally showed well-marked calcification involving particularly the mesial coats. In the Chacma baboon a similar condition of the cerebral vessels was found; the arterial changes in the other two animals of this group were milder in type, and involved chiefly the intima. Necrotic and gliosed foci, atrophic, sclerosed and calcified ganglion cells were present

as the result of vascular deficiency in two of the animals. It would seem, therefore, that cerebral arteriosclerosis, occurring in four of twenty-two animals, is not at all an uncommon condition.

Animal 2.—Chacma baboon (*Papio porcarius*) P. Z. G., 5060. Many arteries, particularly in the basal ganglions, possessed irregularly thickened walls, and distorted, narrowed lumens. The intima appeared normal; the internal elastica was split and reduplicated. In the mesial coat there were more or less hyalinized regions, frequently the seat of calcareous deposits (Fig. 9). The adventitia was usually not involved, but in some instances the muscularis and adventitia were fused and structureless. There were many pale, atheromatous plaques

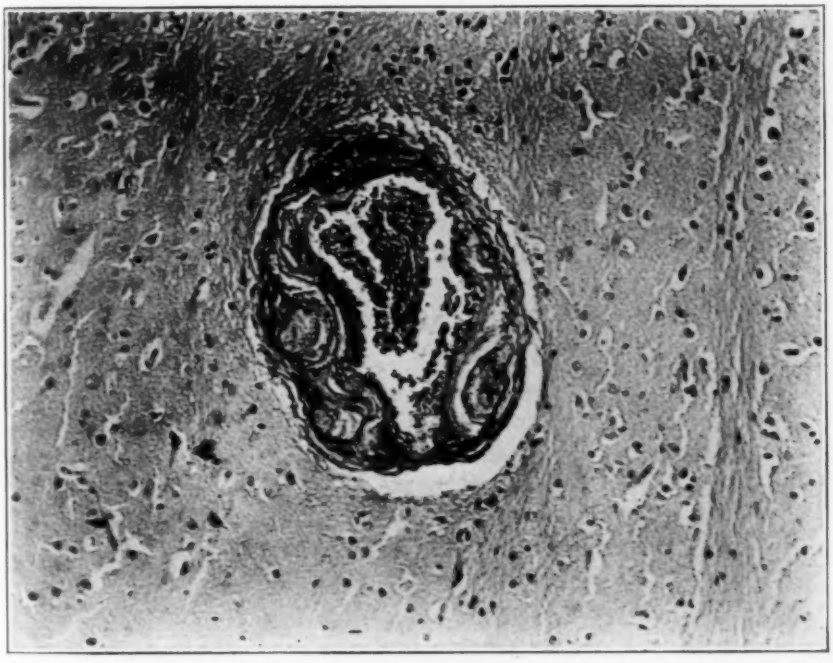

Fig. 9.—Chacma baboon (Papio porcarius), Animal 2. Artery in the basal ganglions. Marked mesial sclerosis, sclerosis of the adventitia, and calcification.

and a diffuse but light incrustation with lime salts. (The other lesions have already been described).

Animal 4.—Pigtailed macaque (*Macacus nemestrinus*), P. Z. G., 5152. The majority of the arteries, in all parts of the brain, had irregularly thickened walls, due to hyalinized, atheromatous or calcified intimal plaques (Fig. 10). The internal elastica was generally split into many fibrils. In the muscular coat there were irregular calcified patches. The adventitia was usually unaffected but, sometimes, calcified patches were present. The smaller arteries and arterioles frequently were transformed into completely calcified tubules, and even some of the capillary vessels were similarly incrusted. Many capillaries possessed irregular, tortuous or angulated, and often bizarre shapes. There were numerous small, irregular foci of degeneration in various portions

of the brain. They usually consisted of a loosely arranged, edematous glial feltwork in which were embedded cellular remnants. Not infrequently such areas were completely calcified. Granule cells, in small numbers, were scattered about the periphery. There was no definite increase of the cellular glia around these foci, but occasionally mild proliferation was found. The ganglion-cells, particularly in the vicinity of the necrosed or gliosed foci, were atrophic and frequently had thick, tortuous processes. The leptomeninges were locally thickened, due to fibroblastic proliferation; collagenous fibrils were plentiful.

Aanimal 5.—White-throated cebus (*Cebus hypoleucus*) P. Z. G., 5354. The subendothelial connective tissue of the intima in a number of pial as well as cerebral vessels was markedly thickened, and hyalinized. This, occasionally,

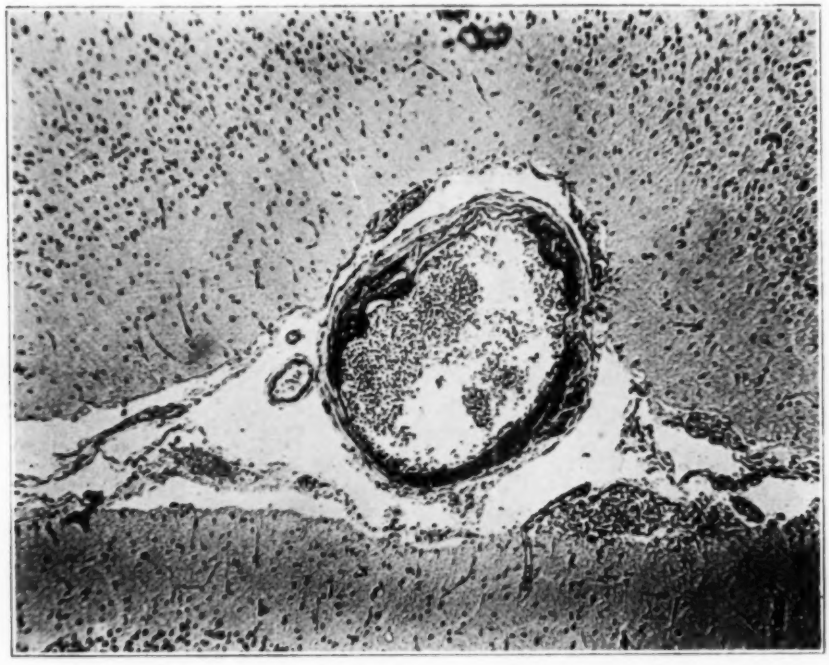

Fig. 10.—Pigtailed macaque (Macacus nemestrinus), Animal 4. Artery in cerebral sulcus. Marked mesial sclerosis and calcification, some thickening of intima.

caused almost a complete obliteration of the vascular lumens. The internal elastica was split and fibrillated; the mesial coats were generally not involved. There was no evidence of calcification, focal necrosis, or gliosis. A number of atrophic and sclerotic ganglion cells were present. In places the pia was mildly thickened and fibrosed.

Animal 6.—Brown cebus (*Cebus fatuellus*) P. Z. G., 5300. A number of small arteries in the sylvian fissure had a moderately proliferated and hyalinized subendothelial intima, and reduplicated, split internal elastica. The mesial coats were normal. A mild, localized fibrosis of the pia was present. No foci of necrosis or gliosis were found. A few ganglion cells were atrophic.

SUPPURATIVE MENINGO-ENCEPHALITIS

This was found in two animals. A very interesting lesion occurred in the night monkey, in which a fairly large abscess of the pons was associated with an acute suppurative leptomeningitis. The animal had lived for only two weeks at the garden and suffered from a "cold" since its arrival. It is, therefore, probable that the infectious agent was conveyed to the brain through the nares. The other animal, a chimpanzee, is said to have suffered from influenza; he had a "cold" and the bacillus of Pfeiffer was cultured from the lungs. The histologic picture was that of mild leptomeningitis with many fibrin thrombi in the pial vessels, and slight mononuclear and polymorphonuclear exudate.

Animal 7.—Noisy douroucouli, "night monkey" (*Aotes vociferans*) P. Z. G., 5127. An oval cyst, 3 by 2 mm. in diameter, occupied the general region of the left pyramidal tract, the mesial fibers of which were destroyed, while the more lateral bundles were still preserved. The cyst was separated from the meninges by a strip of tissue averaging 1 mm. in thickness. Grossly it had smooth walls, but microscopically its periphery consisted of broken-down cerebral substance and numerous pus cells. There was no sharp separation between the definitely necrotic brain substance which constituted its periphery, and the better preserved pontile tissue. Numerous granule cells, degenerated glial and nervous structures were present in the necrotic zone. The leptomeninges over the entire brain were markedly edematous and infiltrated with great numbers of leukocytes embedded in a fine network of fibrin. The cortical ganglion cells exhibited acute degenerative changes. The vessels were moderately engorged and contained excessive numbers of polymorphonuclear leukocytes.

Animal 8.—Chimpanzee (*Pan niger*) P. Z. G., 4157. Pons: the meninges were moderately edematous and slightly infiltrated with large mononuclear and polymorphonuclear leukocytes. Many of the vessels were blocked with a fine fibrin network in which were enmeshed abundant leukocytes. The capillaries of the brain substance were moderately engorged; occasional vessels were filled with fibrin and leukocytes. Now and then the adventitial sheath of a vessel contained a few polymorphonuclear leukocytes. There was considerable acute degeneration of the ganglion cells, but no apparent proliferation of the glia.

TUBERCULOSIS

Only one animal, a sooty mangabey, showed tuberculous infection of the nervous system, a relatively large solitary tubercle being present in the pons.

Animal 9.—Sooty mangabey (*Cercocebus fuliginosus*) P. Z. G., 3962. Pons: adjacent to the sensory nucleus of the left fifth nerve, there was a circular area of necrosis 2 mm. in diameter. The central portions were crumbly and stained lightly with eosin. The periphery consisted of a thin and irregularly arranged wall of large, pale epithelioid cells, between which were found several typical tuberculous giant cells. Encircling the lesion was an indefinite ring formed by scanty numbers of small and large round cells. The smaller elements possessed deep-staining rounded nuclei and but little cytoplasm, the larger cells had fairly abundant cytoplasm and paler nuclei; their cell bodies were indefinite and

faded into the surrounding structures. Similar elements were scattered for some distance through the loose and slightly edematous nerve substance. A small blood vessel with obliterated lumen lay just within the wall of the necrotic area. Elsewhere in the pons there were a number of very small vessels with a few round cells in their adventitial sheaths. The meninges were here and there slightly edematous and infiltrated with occasional round cells.

SUMMARY

Histopathologic study of the brains from twenty-two apes and monkeys disclosed in nine animals, lesions similar to those found in man. Of particular interest was the occurrence, in three animals, of non-suppurative meningo-encephalitis, resembling the lesions of epidemic encephalitis, acute poliomyelitis and certain other diseases. Cerebral arteriosclerosis occurred in four animals, in two of which marked calcification of the vessels and focal areas of necrosis and gliosis were present. In one animal a solitary tubercle was found in the pons. In two animals acute suppurative meningo-encephalitis was present; this was associated in one case with a pontile abscess.

The conclusion may be reached that the interpretation of cerebral lesions in "experimental" monkeys requires caution, since definite "spontaneous" changes were found in over 40 per cent. of the animals studied.

APPENDIX

Pathologic diagnosis of the monkeys from which sections of brain were studied (with the reference number, Philadelphia Zoological Garden):

4992 Orang-utan ♂. Primates, Simiadae, *Simia satyrus*. Ulcerative colitis; cirrhosis of liver with fatty degeneration; mesenteric lymphadenitis; secondary anemia; follicular splenitis; post-nasal catarrhal inflammation.

4157 Chimpanzee ♂. Primates, Simiadae, *Pan niger*. Acute laryngitis; acute bronchitis; bronchopneumonia; acute dry pleurisy; cardiac thrombosis; acute diffuse splenitis; acute catarrhal nephritis; passive congestion and fatty degeneration of liver; acute catarrhal and follicular appendicitis; chronic peritoneal adhesions; pneumococcus and influenza bacilli in culture from lung.

4877 Orang-utan ♀. Primates, Simiadae, *Simia satyrus*. Tuberculosis—caseous of bronchial glands and apex of left lung, miliary of spleen, liver, broad ligament, bronchi and trachea; terminal bronchopneumonia; healed pemphigus in skin.

5060 Chacma baboon ♂. Primates, Cercopithecidae, *Papio porcarius*. Acute diffuse nephritis superimposed on chronic parenchymatous nephritis; acute splenitis; edema of lungs; chronic local pleurisy; acute bronchitis; myocarditis; chronic tonsillitis; chronic duodenitis; hemosiderin pigmentation of intestine.

4244 Yellow baboon ♂. Primates, Cercopithecidae, *Papio cynocephalus*. Osteomalacia. Fracture of humerus. Cloudy swelling of kidneys. Constipation.

5183 Red monkey ♂. Primates, Cercopithecidae, *Cercopithecus patas*. Acute hemorrhagic and follicular enteritis; chronic splenitis; passive congestion and cirrhosis of liver; petechia in lung; cysticercus in liver region.

5374 Squirrel monkey ♂. Primates, Cebidae, *Saimiri sciurea*. Acute diffuse nephritis; worms in cecum.

4196 Brown macaque ♂. Primates, Cercopithecidae, *Macacus arctoides.* Exposure to cold.

5300 Brown cebus ♀. Primates, Cebidae, *Cebus fatuellus.* Chronic interstitial nephritis with retention cysts; fatty infiltration of liver.

5354. White-throated cebus ♀. Primates, Cebidae, *Cebus hypoleucus.* Filaria gracilis in peritoneum; adhesions between intestine and wall of abdomen; perihepatitis; perisplenitis.

5212 Japanese macaque ♂. Primates, Cercopithecidae, *Macacus fuscatus.* Septic osteitis of lower jaw. Cervical lymphadenitis. Chronic follicular splenitis. Focal necrosis of liver (septic).

5042 Pigtailed macaque ♂. Primates, Cercopithecidae, *Macacus nemestrinus.* Diffuse nephritis; tuberculosis of lung; fly larva encysted on capsule of kidney.

5152 Pigtailed macaque ♀. Primates, Cercopithecidae, *Macacus nemestrinus.* Acute infection; necrosis of liver; congestion of spleen; mesial aortitis; fatty degeneration of kidney.

5347 Pale cebus ♀. Primates, Cebidae, *Cebus flavescens.* Ileus; adhesions of rectum to stomach due to tapeworms in large intestine and rectum; anemia; filaria gracilis in peritoneum; filaria in lung; petechial hemorrhages in stomach; perisplenitis; congestion of kidney.

4847 Humboldt's woolly monkey ♀. Primates, Cebiadae, *Lagothrix lagotricha.* Chronic ulcerative enteritis with acute exacerbation; acute lymphadenitis.

5127 Noisy douroucouli ("Night Monkey") ♂. Primates, Cebidae, *Aotes vociferans.* Atrophic enteritis; congestion of kidney; fatty infiltration of liver.

189 Rhesus macaque. Primates, Cercopithecidae, *Macacus rhesus.* Still born.

4275 Rhesus macaque ♂. Primates, Cercopithecidae, *Macacus rhesus.* Multiple infected subcutaneous wounds; cloudy swelling of liver with fatty degeneration; hyperplasia of spleen with local congestion; pigmentation of lymph-nodes; general obesity; pneumonosis foci in lung; subacute catarrhal bronchitis.

3962 Sooty mangabey ♂. Primates, Cercopithecidae, *Cercocebus fuliginosus.* Generalized tuberculosis; ulcerative proctitis (tuberculous); acute catarrhal gastro-enteritis; acute degenerative nephritis.

3196 Weeper cebus ♀. Primates, Cebidae, *Cebus capucinus.* Organs healthy.

5161 Black spider monkey ♀. Primates, Cebidae, *Ateles ater.* Ulcerative colitis (amebic); chronic hyperplasia of spleen; acute nephritis; fatty infiltration of liver.

4636 Entellus monkey ♂. Primates, Cercopithecidae, *Presbytis entellus.* Portal cirrhosis of liver; passive congestion of intestine with hemorrhage into duodenum; acute diffuse nephritis; hypostatic congestion of lung.

CHRONIC INTESTINAL AMEBIASIS

CLINICAL ASPECTS WITH SPECIAL REFERENCE TO NEUROPSYCHIATRIC MANIFESTATIONS

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The very extensive literature [1] on the subject of intestinal amebiasis, during the past ten years particularly, indicates the growing importance of this type of infection in temperate climates as well as in the tropics.

The reports of the Medical Research Committee of Great Britain [2] show the great prevalence of chronic dysentery in returned soldiers, not only among those who have been in tropical regions, but even more so among those who were in France. The conclusions of this Committee are that these men are no longer fit for active military life because of the return of symptoms when proper care and diet are impossible.

These reports also call attention to the miserable health of many of these men, most of the time, and the difficulty of effecting a complete cure. For example, among ninety-six cases fifty-seven were "cured," but thirty-six relapsed. It is interesting to note that in most cases of chronic amebic infection, diarrhea is not present, but rather a chronic constipation; and that without careful stool examination the infection may be overlooked.

This paper is in the nature of a preliminary report on twenty-five cases of intestinal amebiasis, all of which were in exservice men and were referred to the writer primarily because of symptoms regarded by prior examiners as neurologic or psychiatric.

The following tables in which these cases are summarized will show the frequency of the neurasthenic syndrome and in some cases a neuritic and arthritic syndrome. The analysis of the principal symptoms presented by these patients will indicate how easily many of them would have been classed as psychoneurotics until a complete physical examination, including the stool examination, was made.

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1. Editorial: J. A. M. A. (May 21) 1921; Kofoid, C. A.; Kohnhauser, S. I., and Plate, J. T.: Intestinal Parasites in Overseas and Home Service Troops of the U. S. Army, J. A. M. A. **72**:1721 (June 14) 1919; Kofoid, C. A., and Swezy, Olive: On the Prevalence of Carriers of Endamoeba Dysenteriae Among Soldiers Returned from Overseas Service, Am. J. Trop. Med. **1**:41 (Jan.) 1921.

2. Reports of Medical Research Committee of Great Britain, London: Nos. 7 and 29.

TABLE 1.—*Symptoms and Effects of Treatment in Intestinal Amebiasis*

Case	When and Where Infected	First Symptoms	Secondary Symptoms and Signs	Duration Before Ipecac Treatment	Prior Diagnoses	Organisms Found in the Stools	Effect of Ipecac Treatment
1	France, 1918	Diarrhea	Feeling of suffocation at night; palpitation of the heart; restless feelings; emotional irritability; poor vasomotor tone; fine tremor of hands; basal metabolism 20+	Free interval of two years, followed by secondary symptoms	Toxic thyroid; psychoneurosis	Amoeba histolytica	Ipecac adsorption product; improved promptly
2	Philippine Islands, 1916	Severe diarrhea	Marked physical asthenia; constipation; flatulence; and rapid heart action	4½ years	Toxic goiter; myocarditis	Amoeba histolytica	Adsorbed ipecac produced immediate benefit, felt well six months later
3	France, October, 1918	Acute and recurrent attacks of diarrhea	Poor appetite; chronic constipation; headache, dizziness and blurred vision occasionally; cannot do hard work as formerly; chronic aching pains in the upper dorsal and cervical spine, with extreme sensitiveness to pressure over the large nerve trunks in all extremities; roentgenograms show calcified deposits in the foramina of the upper dorsal vertebrae; Wassermann reaction negative	2½ years	Dysentery; neurosyphilis; arthritis	Amoeba histolytica	Immediate temporary relief from pains but after five months of adsorbed ipecac the arthritis had progressed; no benefit from emetin injections; recurrent diarrhea with blood
4	France, 1918	Severe diarrhea with bloody stools	Insomnia; nervousness; lack of energy; poor appetite; occasional diarrhea; often vomits after breakfast	2½ years	Sequelae of influenza; neurasthenia	Many motile forms of Amoeba histolytica	No marked benefit from emetin and adsorbed ipecac; stool positive
5	Philippine Islands, 1919	No diarrhea, only nervous irritability	Nervousness with crying spells; feeling of inadequacy; frontal headache; insomnia; anxiety about himself; cold extremities; no organic signs	18 months	Neurasthenia following influenza	Amoeba coli; Amoeba histolytica	Improved in all respects but still rather nervous after five months adsorbed ipecac treatment
6	France, September, 1918	Acute diarrhea	Cold, bluish, moist hands; bright red tongue; lack of physical and mental energy; alternating constipation and diarrhea	2½ years	Chronic entero-colitis	Amoeba histolytica	Improvement at once after emetin (6), neo-arsphenamin (3), emetin iodid (36 grains); feels well, stools negative
7	France, 1918	Diarrhea	Pains in muscles of back and chest; poor appetite; nervous and easily tired; mental activity slowed; underweight	2 years	Intercostal neuralgia; muscular rheumatism; neurasthenia	Amoeba histolytica	Improved by adsorbed ipecac very promptly and entirely relieved of distress

TABLE 1.—*Symptoms and Effects of Treatment in Intestinal Amebiasis—(Continued)*

8	France, 1918	Mild diarrhea and abdominal pains	Lack of energy; distress in upper abdomen; inability to concentrate; feeling of apprehension; insomnia; blood pressure, systolic 110, diastolic 60; Wassermann reaction negative; no signs of organic nervous disease	2½ years	Chronic appendicitis; neurasthenia; hysteria	Amoeba histolytica	Unimproved by three weeks of adsorbed ipecac; treatment not persisted in when sent to hospital
9	United States in 1914	Diarrhea	Chronic pains in upper spine and the shoulders; roentgenograms show hypertrophic changes in the cervical vertebrae; teeth negative	7 years	Arthritis	Many specimens of Amoeba histolytica	Improved slowly under adsorbed ipecac and physiotherapy
10	France, 1918	Bloody and loose bowel movements	Marked feeling of mental inadequacy causing nervousness and emotional depression; lack of physical energy and inability to do usual work as a salesman; signs of myocardial atony; pyorrhea and dental caries	2½ years	Tuberculosis; myocarditis; intestinal toxemia	Amoeba histolytica	Improved but cannot eat regular diet
11	Cuba, 1916	Diarrhea	Nervous; lacking in energy; painful and sometimes bloody bowel movements, but is usually constipated	5 years	None made	Many specimens of Amoeba histolytica	Able to digest food better, not in normal health
12	France, September, 1918	Acute diarrhea	Headache, difficulty in concentrating; irritable; tires easily; flatulence; chronic constipation; chronic pains in upper dorsal spine and neck	2½ years	Ptomaine poisoning; gastritis; tabes dorsalis	Amoeba histolytica	Unimproved after taking 600 tablets of adsorbed ipecac in dosage of 9 per day; stool still positive; arthritis and pains in legs continue
13	Camp Lewis, January, 1918	Diarrhea for three months	Alternate constipation and diarrhea; very irritable; often depressed and hyperemotional; feeling of inadequacy always since first symptoms and hence nervous when talking to people and unable to resume former work; went through the war by force of will but could do nothing after the armistice	3 years	Not made definitely but considered a psychoneurosis	Many specimens of Amoeba histolytica	Stools positive after vigorous combined treatment; subjective symptoms only slightly improved; gastro-intestinal symptoms the chief residuum
14	Allentown, Pa., August, 1917	Diarrhea	Difficulty in mental concentration; easily fatigued and depressed; "tired" most of the time	3½ years	None made	Amoeba histolytica	Improved
15	Camp Dix, N. J., August, 1918	Diarrhea	Flatulence and constipation; headaches; and nervousness	2½ years	Gastritis	Amoeba histolytica	Improved
16	France, 1918	Severe diarrhea with bloody stools	Frequent constipation; lack of energy; coated tongue; pain in abdomen after eating usual diet; 20 pounds loss in weight; poor circulation in extremities	2 years	Enterocolitis; "run down"	Amoeba histolytica	Under adsorbed ipecac and emetin he showed no improvement; after a year of intermittent treatment, stools were positive

Case	When and Where Infected	First Symptoms	Secondary Symptoms and Signs	Duration Before Ipecac Treatment	Prior Diagnoses	Organisms Found in the Stools	Effect of Ipecac Treatment
17	Camp Lewis, 1917, and France, 1918	"Run down" and nervous; no diarrhea	Nervousness; easily tired; disseminated choroiditis; no signs of organic nervous disease; negative Wassermann reaction	2 years	Dementia praecox; neurosis; syphilis, and choroiditis	Amoeba histolytica	Improved quickly in general subjective symptoms
18	France, 1918	Diarrhea	Periodic nausea; anorexia and vomiting about once in four months and lasting for two weeks; occasional loose bowel movements	2½ years	"Gassed"	Amoeba histolytica	With emetin and neo-arsphenamin improved promptly; well after two months
19	Camp Meade, 1918	Severe diarrhea	Unable to work as a clerk because of dizziness; weakness; flatulence; chronic constipation; cardiac tone defective; pulse pressure 50	2½ years	Sequelae of influenza; myocarditis	Amoeba histolytica	Improved quickly with adsorbed ipecac only, but not in normal health after six weeks treatment
20	France, 1918	Acute diarrhea	Nervousness; indigestion; constipation; lack of mental concentration; insomnia; restless and depressed; poor peripheral circulation; cannot work; thyroid diffusely enlarged	2½ years	Hyperthyroidism; neurasthenia	Amoeba histolytica	Stool positive, but much improved and promptly relieved by large doses of adsorbed ipecac; able to work, good appetite, gained 12 pounds
21	Philippine Islands, 1914 to 1917	Diarrhea	Nervousness; insomnia; chronic fatigue; poor appetite; abdominal pains and nausea after eating in recurrent attacks, with remissions	5 years	Pes planus only	Amoeba histolytica	Slightly improved with adsorbed ipecac
22	France, July, 1918	Acute diarrhea, also "gassed"	Nervousness; general weakness; recent loss of 20 pounds weight; poor appetite and chronic constipation	2½ years	"Gassed"	Amoeba histolytica	Improved quickly with adsorbed ipecac
23	France, 1918	Acute dysentery	Frequent constipation; flatulence; occasional diarrhea; difficulty in mental concentration	2½ years	Amebiasis	Amoeba coli; Amoeba nana; Amoeba histolytica	Improved
24	France, October, 1918	Acute diarrhea	Easily fatigued; feels "worn out" all the time; underweight; cold purple hands; constipation alternating with looseness of bowels	2½ years	Arrested tuberculosis	Amoeba histolytica	Improved
25	France, October, 1918	Several attacks acute diarrhea	Nervousness; insomnia; constipated; cannot eat regular diet without having a headache	2½ years	None made	Amoeba histolytica	Much improved; feels well while taking adsorbed ipecac

TABLE 2.—*Summary of Cases Detailed in Table 1*

Prior Diagnoses (all finally referred as neuropsychiatric):		
Toxic goiter	3	
Psychoneurosis	2	
Neurasthenia	6	
Hysteria	1	
Myocarditis	3	
Neurosyphilis	1	
Arthritis (cause not specified)	2	
Enterocolitis	2	
Intercostal neuralgia and muscular rheumatism	1	
Chronic appendicitis	1	
Tuberculosis	2	
Ptomaine poisoning	1	
Tabes dorsalis	1	
Gastritis	2	
Dementia praecox	1	
Gassed	2	
Amebiasis	1	
No diagnosis	3	
Total different diagnoses, 17		
Average duration of infection before final diagnosis		2.9 years
Principal Symptoms—Subjective and Objective:		
Nervousness	17	
Constant fatigue	25	
Feeling of social inadequacy and melancholy	6	
Insomnia	6	
Irritability	6	
Anxiety feelings—with palpitation	3	
Poor mental concentration	9	
Chronic constipation	15	
Diarrhea	5	
Headache and dizziness	5	
Peripheral nerve pains	5	
Enlarged thyroid	1	
Cold and cyanotic extremities	5	
Effects of Ipecac Treatment:		
Symptomatically cured	5	
Symptomatically improved	13	
Symptomatically unimproved*	7	

* Least benefit in the two arthritic cases.

COMMENTS

In all patients presenting symptoms which might be ascribed to psychologic causes, an attempt was made to discover any causative mental complexes but without result. Accompanying the subjective symptoms of a generalized functional disturbance of the nervous system were objective signs indicating a toxic condition. For example, attention is called to the frequency of vasomotor disturbances: cold and cyanotic extremities, excessively perspiring hands, and signs of cardiac irritability.

The data were tabulated nearly a year ago. Since that time several of the patients have been seen from time to time and are still complaining of digestive disturbances and lack of normal energy. In one, a manic-depressive psychosis has occurred. This is the only instance of actual psychosis developing in any of the group. This patient was one of those who had a severe upper dorsal arthritis.

While other factors than intestinal infection may have contributed to some of the symptoms found in these patients, there is enough uniformity of symptoms and signs to warrant calling attention to intestinal amebiasis as a factor in chronic illness of the "neurasthenic" type.

With reference to the arthritic cases, in both the roentgen-ray revealed calcareous deposits in the foramina of the vertebrae at the levels from which referred pains radiated.

SUMMARY

Twenty-five cases of amebic infection with *Endamoeba hystolytica* had the following syndromes in order of frequency:

1. Neurasthenic syndrome with mental depression.
2. Toxic syndrome with myocardial irritability simulating hyperthyroidism.
3. Polyneuritic syndrome.
4. Arthritic syndrome with reflex nerve pains and deposits in foramina of the vertebrae.

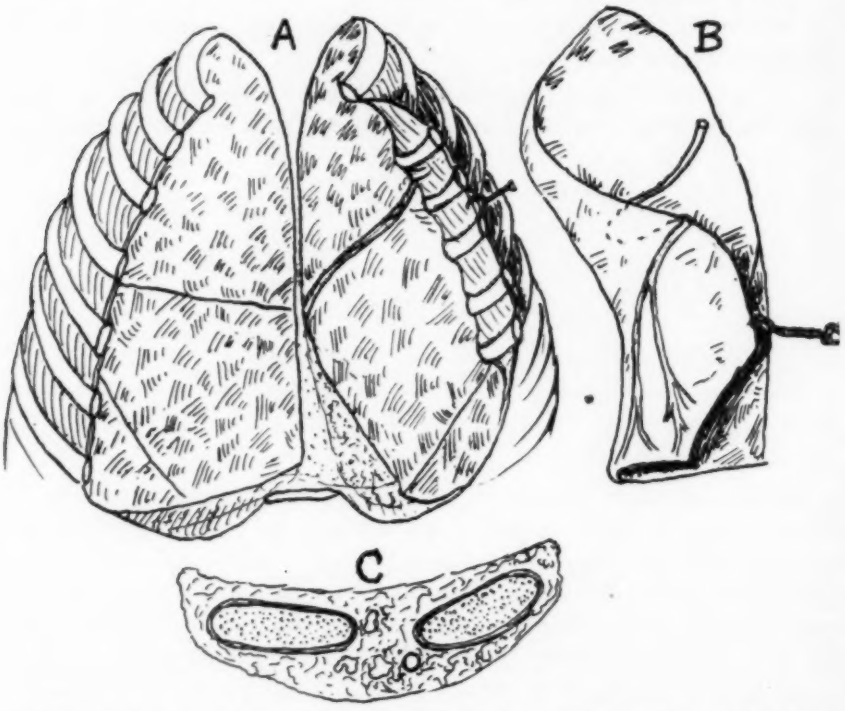
All presented gastro-intestinal syndromes characterized by poor appetite, flatulence and chronic constipation, with occasional diarrhea.

Occasional Notes

INTERCOSTAL NERVE VARIATIONS

From the Anatomical Laboratory of the Medical Department of the State University of Iowa, I report two cases of intercostal nerve variation. The first case is illustrated, the second is not.

The second intercostal nerve on the left side gave off a large branch opposite the midaxillary line. This nerve pierced the internal intercostal muscle and then attached itself to the pleura, as the phrenic nerve does. Coursing over the pleura (*A* in the accompanying figure), it arched around its anterior border to run down on the mediastinal pleura towards the diaphragm. On this



Second intercostal nerve in Case 1: *A*, anterior surface of pleura; *B*, nerve branching on mediastinal surface; *C*, transverse section of main nerve trunk.

mediastinal surface it divided into two branches (*B* in the accompanying figure). A section of the main trunk was removed and histologically sectioned: it showed two distinct nerve trunks, with well indicated myelinated nerve fibers (*C* in the accompanying figure).

The second specimen was much the same, excepting that a branch came from the third intercostal, and one from the fourth intercostal nerve. These two trunks on being sectioned histologically showed only one nerve trunk each.

These conditions are of interest in relation to referred pain.

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Abstracts from Current Literature

MULTIPLE SCLEROSIS AND ITS ETIOLOGY. E. Long, Schweiz. med. Wchnschr. **53**:109 (Feb. 1) 1923; Rév. méd. de la Suisse Rom. **43**:27 (Jan.) 1923.

This article is an introduction to an official inquiry into the frequency and dissemination of multiple sclerosis in Switzerland.

According to the author, multiple sclerosis is more prevalent in Switzerland than was formerly supposed. Pathologically, multiple sclerosis presents reddish gray plaques scattered throughout the nervous system. These vary in size, are usually superficial and involve the white substance. They may at times be situated centrally. These sclerotic lesions usually appear as sharply defined areas, but when stained by the Weigert-Pal method show no sharp demarcation. The plaques also occur in the brain, medulla, pons, cerebellum and basal ganglions, both in the white substance and in the cortex. The retina and optic nerve, as also the olfactory bulb and other cranial nerves, are affected. The anterior and posterior spinal roots and the cranial nerves for a distance from the brain may show involvement. There is no definite evidence of peripheral nerve change so that one may say the condition is limited to the central nervous system and especially to the neuroglia.

Longitudinal sections through the cord reveal that the nerve fibers between two adjacent plaques show no change. Secondary degeneration does not occur. The nerve fibers, while losing their myelin sheaths, retain their trophic functions, and after the disappearance of the plaques, they again resume their normal structure. The ganglion cells in a plaque show but little change. There may be a chromatolysis but they retain their nuclei and nucleolus. These are the important facts to bear in mind in order to understand the physiologic mechanism of this disease.

It is clear that under these criteria a multiple sclerosis can appear clinically only when there are sufficient plaques, well enough localized, to bring about clinical signs. In the formes frustes, plaques will be found by the hundreds scattered throughout the central nervous system. It was long held that the sclerotic plaques were sclerogliotic foci, but this is no longer tenable. It is true that the glia forms a thick network, but the nerve fiber loses only its myelin sheath, the axis cylinder being only affected to a minor degree. The ganglion cells, as already noted, are only slightly, if at all, involved. Interstitial substance may show a slight inflammatory change. There may occasionally be some vascular infiltration. Considerable variation occurs and it may happen that no change is noted. It may be said that one has to deal with a disease of the central nervous system, characterized by scattered foci of gliosis, varying in size and age and containing marked and deformed axis cylinders. According to some authorities the glial changes are primary; according to others, and the more modern, the parenchymal changes are primary, and only secondarily produce changes in the glial and connective tissue structures. The anatomic changes tend to explain the clinical observations. The insidious progress with exacerbations are compatible with the changeability of symptom complexes due to plaques occurring in various parts of the central nervous system. Charcot described three clinical forms, the cerebral, the spinal and

the cerebrospinal. He also called attention to the rudimentary and atypical forms. Besides his work, Muller, in 1904, and Oppenheim, in 1914, described the disease very thoroughly. The spinal form may be cervical, dorsal or lumbosacral in its onset. It may affect mainly the lateral columns or the posterior columns, the motor or sensory areas of the cord. In the cerebral form there are naturally more possibilities of localization and more complex pictures may occur. The two chief types are the paralytic and the type of incoordination. The paretic, spastic condition is almost constant. Motor power is usually diminished with an increase of deep reflexes and Babinski phenomena. The cremasteric reflexes are diminished, while the abdominal reflexes are nearly always absent. The latter is so constant that some authorities consider this one of the principal signs of the disease.

If the motor impairment is more marked, paraplegia or tetraplegia, and more rarely hemiplegia occur. A plaque may involve a spinal root or cranial nerve nucleus with resulting paralysis. The optic nerve is not infrequently affected, causing a characteristic optic atrophy.

It was formerly assumed that sensory disturbances did not occur in multiple sclerosis. This, however, is not true. They are not uncommon, but are usually not severe. Paresthesias (very persistent pains) may occur; bladder disturbances are not infrequent.

Disturbances of coordination are very significant. Every student is told of the importance of the intention tremor, the scanning speech and the nystagmus. The tremor is of importance as it may lead to a wrong diagnosis. It is not a regular or rhythmical tremor, but is the result of incoordinate movements which occur especially at the end of a volitional or intentional act. It gradually increases and by persistence may even become more marked. The scanning speech and the nystagmus are synergic disturbances; the ataxia a cerebellar incoordination. The symptoms are due to a cerebellar lesion or lesion in the cerebellar tracts. Charcot pointed out that one must not rely too much on these signs, for as Nonne, Bing and others have shown, only about ten to fifteen per cent. of the cases are at all typical.

The motility disturbances of multiple sclerosis may be divided into three large groups: (1) In a large number of cases there is marked spasticity with impairment of movement in the lower or all four extremities, but without any definite incoordination. This represents the spinal form and may present difficulties in differentiation from syphilis of the cord, especially if there are sensory changes and bladder disturbances. At necropsy, the plaques in some cases appear to be more localized in the cord. However, in the majority of cases the lesions appear in the brain and in the pyramidal tracts, causing a diplegia. (2) If incoordination of movements is added, then one sees the spastic cerebellar type which may be considered the classic type. This combination is not always found. Clinically one more frequently finds cases of multiple sclerosis which have disturbances of equilibration or incoordination of the limbs, in which, even though the condition is advanced, no scanning speech is noted. (3) If signs of paralysis or changes in reflexes are absent and only cerebellar signs present, one sees the typical cerebellar syndrome. This is not rare, but usually is only an early condition, as later, spasticity appears. In the cerebellar forms there is noted a great variation of symptoms and in some cases it requires a thorough investigation to determine which movements have become ataxic.

The classification into three groups is only feasible when it is understood that in the cerebral type the cerebellum is also involved.

Occasionally a mild muscular atrophy, especially of the distal parts, may be present. While this is rare, it is important as it may lead to an incorrect diagnosis of amyotrophic lateral sclerosis.

Even more important than the variability of the symptoms, is the variability of the course of the disease. Acute, subacute and chronic types are described. The acute type which ends in death in a few months is rare. The main difference between the subacute and the chronic is the duration, the latter lasting up to twenty or more years. A gradual progression is rare, periodic increase of symptoms and remission are the rule. The exacerbations may be sudden or gradual; they may be apoplectic in character or associated with vertigo and vomiting. The remissions are variable in duration, up to fifteen or twenty years have been recorded. It is doubtful if the condition ever remains stationary as the time usually seems to come when the disease process again advances. The remissions may not incorporate the entire clinical picture, but may be confined to isolated symptoms such as paralysis of the eye muscles or facial muscles. The optic atrophy does not lead to blindness as in tabes, the amblyopia usually becomes less and changes from one eye to the other. The patient's ability to continue work is naturally very variable.

Psychologically one speaks of transient confusional periods which may lead to a psychotic state. Euphoria is often very noticeable in the progress of the disease. Self-criticism is not infrequent; this is usually in a humorous vein. In the end stages, prior to coma, there is a carelessness and euphoria, somewhat resembling general paralysis without the loss of memory.

The disease usually terminates by a state of immobility, with cachexia and decubitus, or by bulbar disturbances, which hasten the exit. All in all, the symptomatology is so variable that for differential diagnosis one would have to review the pathology of the entire central nervous system. Diagnosis is usually uncertain before the clinical signs are well established. At present, with the aid of lumbar puncture, the differential diagnosis is made easier. Lymphocytosis is rare; if present, an inflammatory condition must be considered. The Wassermann reaction is negative.

The etiology still remains unsolved. Marie first suggested a nonspecific toxic basis, as typhus, measles and even syphilis; lead, arsenic and mercury have also been incriminated. Strümpell then suggested a neurotrophic developmental disorder, but this has not stood the test of time. In 1917, Kuhn and Steiner, and in 1919, Marinesco thought they had found spirochetes which were believed to be the cause of the disease. This has not been substantiated. In 1922, Pettit considered the disease due to a specific virus, but little proof has been brought forward in this direction. The therapy, unfortunately, even with the advent of arsphenamin and other preparations, has proved uniformly unsuccessful.

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STUDIES IN EXTRAPYRAMIDAL SYNDROMES; PROGRESSIVE INFANTILE TORSION SPASM (SYNDROME OF THE CORPUS STRIATUM). A. WIMMER, Rev. neurol. **28**:952 (Sept.-Oct.) 1921.

The article is based chiefly on the clinical and necropsy findings in a girl twelve years of age. The case, before coming to the psychiatric clinic of Wimmer, was diagnosed in the neurologic polyclinic of the Rigs hospital, as a severe hysteria. The notes at that hospital describe her as having "an embarrassed speech" and a trembling, hesitating gait; she was unable to stand

erect; she walked slowly, leaning on the arm of her nurse, in short steps, spastic and almost like an automaton; on one occasion, she walked on all fours. From time to time she showed choreiform tremors of the extremities with a tendency to rigidity of movement. At times she appeared frightened and at others apathetic. She smeared herself while eating. No difficulty in swallowing was noted. She was quite emaciated. Opthalmoscopic examination was negative. The blood Wassermann reaction was negative; spinal puncture revealed: cells 4, globulin negative, Bordet-Wassermann test negative. There was a right otitis media. Such were the findings with a diagnosis of hysteria before the patient was admitted to Wimmer's service.

Wimmer's examination is very detailed and includes: a careful history, both of the patient, and her family; a careful psychiatric and neurologic examination; the muscle status and the general physical condition, as well as the usual laboratory studies. The clinical chart showed a moderately rapid progression. The bodily contortions became more and more acute; there was a continuous increased motor agitation; great emaciation in spite of long-continued good appetite. Toward the end of her residence in the hospital there was a recrudescence of the otitis, accompanied by irregular elevations of temperature. Later she developed a deep abscess in the lumbar region following pneumonia, and finally died, Aug. 1, 1920.

Abstracting the main features in the case, we find a negative family history for nervous and mental diseases or for a disorder similar to that of the patient in other members of the family, and there was no evidence of congenital syphilis. The clinical course presented two important features: (1) bizarre attitudes and grotesque contortions of the body and of the extremities. These were never absent, not even during sleep; (2) marked increase in the general motor excitability. The choreiform movements and contortions were involuntary in character and involved almost all the muscles of the body.

Although there were speech difficulties, there were no general spasticity nor paralyses. The reflexes were not exaggerated; there were: no Babinski sign, no sphincter trouble, no sensory disturbances, no ocular symptoms, no lesion of the optic nerve, and no nystagmus. Finally, there were no psychic symptoms nor general cerebral symptoms. Hysteria might well have been accepted as a diagnosis except for the following important features: the abnormal and grotesque attitudes persisted during sleep; the course of the disorder was rather long (2 years) for a child so young. According to the author infantile hysteria or hysteria in children is usually monosymptomatic, and yields readily to isolation of the patient.

The writer thought, from the first, that in this case he was dealing with an "extrapyramidal encephalopathy," a "syndrome of the corpus striatum," and a case not to be confused with a so-called "double athetosis," or S. A. K. Wilson's syndrome. He thinks it more like Oppenheim's "dysbasia lordotica progressiva v. dystonia musculorum deformans," or like the case described by Thomalla in 1918, a case of "torsion spasm," in which necropsy revealed a "bilateral lesion, a total necrosis of the putamen, and hepatic cirrhosis," changes showing essentially the same pathologic picture as the syndrome of Wilson's disease.

The author then submits his necropsy findings. In touching on the microscopic findings in the brain sections, he states that the most remarkable changes are those in the neuroglia, which, in every part of the brain examined, correspond exactly to the changes described by Alzheimer in a case of pseudo-

sclerosis. Photographic plates, fourteen in number, follow. His description of these plates concludes with the statement that no portion of the brain examined exhibits evidence of inflammation or vascular change.

The author believes his case to be the second, which demonstrates that the "torsion neurosis" is (or may be) an organic affection, a "syndrome of the corpus striatum," which is closely related to Wilson's disease with a characteristic hepatic pathology. Moreover his case shows not only striate involvement, but also diffuse alterations in the brain substance, which, from a histopathologic point of view are analogous to changes in the striate body. These diffuse changes, including, by the way, the lenticular nucleus as well, is what suggests the descriptive term pseudosclerosis. He quotes Spielmeyer as having demonstrated, as late as 1920, that the two clinical syndromes which we designate as Wilson's disease and pseudosclerosis are from an histopathologic point of view essentially one and the same thing.

He then raises the question as to whether the involvement of the striate body determines the principal symptoms in his case. This cannot be exactly determined, for, while the striate body influences muscle-tone, yet it is but a part of a more extended system, namely, the cerebellorubrothalamofrontal system which in turn controls subcortical motor mechanisms and muscle tone. It is for this reason that one may arrive at certain erroneous and risky conclusions concerning lesions of the corpus striatum; e. g. we find certain beautiful cases of Wilson's disease complicated with pronounced lesions of the dentate nucleus. The same thing may be said of cases published recently in Denmark involving the thalamus in which there is "general muscular rigidity and a paralysis agitans," but which nevertheless show no involvement of the striate body.

The paper concludes with the opinion that different clinical pictures are the result chiefly of a difference in the combination in the same cerebropathy. The rapidity of the disease, the stage it has reached, and the age of the brain all play a part in the manifest variations.

JONES, Detroit.

ANGIOSPASM IN VASOMOTOR AND TROPHIC NEUROSES. FRITZ BRÜNING, Deutsch. med. Wchnschr. **48**:1572 (Nov. 24) 1922.

The significance of angiospasm in the pathogenesis of the vasomotor neuroses is well known. Under this head Cassirer mentions acroparesthesia, erythromelalgia, Raynaud's disease, scleroderma, acro-asphyxia, etc.

Raynaud very early assumed that local syncope, the forerunner of local asphyxia, was the result of contraction of the small arterioles and also of the larger arteries. Until recently the transient contracture of blood vessels has been the only intra vitam evidence of angiospasm. Pathologic investigation has shown a generalized deficiency of the vascular system or a hyperplasia of the arteries, and from this it has been assumed that the vascular spasm causes the hyperplasia.

Brüning has shown that angiospasm extends high into the arm, even into the brachial artery; this was demonstrated at operation for periarterial sympathectomy. He feels that the operation of Jaboulay and Leriche has a very definite application in the vasomotor trophic neuroses. Three cases are reported:

1. A woman, aged 47, had marked vasomotor trophic disturbance in the right hand with constant pain. The operation in this case was a periarterial sympathectomy of 10 cm. on the brachial artery. The artery was found to

be small, about the size of the radial artery. Pulsations could not be felt here, although they were present in the radial artery. For a distance of 7 cm. the adventitia was stripped away. During the operation it was observed that the artery contracted to about one-half its normal size except where the adventitia was removed; here it remained unchanged. At the same time the radial pulse disappeared and did not return during the entire operation. Six hours later the radial pulse was again palpable. The pain rapidly disappeared and trophic disturbances cleared away. Four months later the hand seemed perfectly well.

2. A woman, aged 57, with scleroderma. On both hands the skin was markedly leathery. There was itching and prickling pain in the fingers. Operation on the right brachial artery was performed. Two months later marked improvement was noted. There was no pain and the patient could use her hands quite well.

3. A man, aged 23, who had a spastic paraplegia following transverse myelitis, the result of Pott's disease. There was beginning trophic disturbance of the feet and toes. The right femoral artery was exposed and sympathectomy was done. Within fourteen days considerable improvement was noted.

The author also reports two cases of Raynaud's disease treated in the same manner by Kummell and one by Lotschs. In these six cases the outstanding finding was a spasm of the arteries. Brüning feels that this is not a congenital condition but the result of spasm. He gives the following reasons: the existence of palpable change in the radial artery; the change in caliber of vessels in intermittent claudication, which has been observed by Wieting at operation; the results obtained by sympathectomy; and the observation noted in Case 1 in which the pulse could not be felt in the field of operation but could be felt in the radial artery. As the sympathectomy relieved the vascular spasm, the author assumes that one is dealing with a disturbance of the sympathetic nervous system; and, moreover, that the vascular spasm is not of myogenic but of neurogenic origin.

The author sees in an angiospasm a symptom of increased tonus of the sympathetic nervous system. Sympathectomy does not cure the disease (e. g., Raynaud's) but relieves the symptoms by decreasing the vascular tonus. To what degree the so-called trophic functions are affected remains an open question especially as we do not know if there are nerves with trophic function alone.

Sympathectomy is a most helpful adjunct. If some operators have not been successful, this may be attributed to errors in technic and the selection of cases. With experience one should be able to select cases very effectively.

For the present the author presents the following indications for sympathectomy: (1) all vasomotor trophic neuroses associated with an angiospastic condition; (2) angiospastic conditions in the presclerotic period of arteriosclerotic gangrene and intermittent claudication; (3) possibly frost gangrene and end-arteritic gangrene because of the secondary hyperemia which follows the sympathectomy; (4) trophic changes resulting from nerve injuries if no results are obtained or are possible by neurolysis or nerve section.

Sympathectomy is contraindicated in embolic and diabetic gangrene.

It is certainly true that the earlier these cases are operated on, the better the results will be. It is especially desirable to operate while the vessels are still in a state of transient spasm, as then permanent changes probably have not occurred. The results obtained by sympathectomy indicate that vasomotor trophic disturbances are not so much caused by loss of nerve

function as by increase in the irritability of the nervous system. The author briefly describes the operative technic. He states that the operation should be performed at as high a point as possible and that about 8 cm. of the artery must be isolated and the adventitia removed. If the disturbance is traumatic in origin, the exposure must be well above the site of injury.

MOERSCH, Rochester, Minn.

ANATOMIC AND FUNCTIONAL RESULTS OBSERVED IN THE COURSE OF CICATRIZATION OF NERVES IN THE DOG. L. GUYON, Rev. neurol. **28**:937 (Sept.-Oct.) 1921.

The paper is based on a series of studies undertaken at the Collége de France and at the Salpêtrière with especial reference to the comparative value of end-to-end suture and grafting with dead nerves. The conclusions are based on experiments on sixteen dogs in which the experimenters cut the two branches of the sciatic or of the internal popliteal nerve alone. Two sutures in the nerve sheath suffice to hold the ends of the nerve in coaptation. The cicatrices are fixed or set in paraffine and cut far enough above and below the lesion (where the nerve was originally cut) to allow a careful counting and measurement of the fibers.

The muscles are studied in two groups, one supplied by the internal popliteal branch of the sciatic and the other by the external popliteal. For the fibers in a normal state the authors give 2:46 as a ratio between those of the internal and the external popliteal. They also give norms for the muscles supplied by both branches of the sciatic. These norms or ratios are followed by a series of observations on the sixteen dogs made after suture or graft at intervals of from forty-three days to a year. These observations include anatomic details of the nerves above and below the cicatrix, the condition of the muscles and the relations which exist between nerve regeneration and muscular restoration, as well as a comparison between the results in end-to-end suture, and nerve graft.

State of the Nerve Above the Cicatrix.—Two conditions may result from section of the nerve: regeneration follows, or does not follow, degeneration above the point of section. Moreover, in case of regeneration, we find two conditions: The fibers that regenerate are usually smaller and somewhat scattered, and there are certain fibers that show only the empty sheath; in other words we have the phenomenon of total destruction and of the multiplication of nerve fibers of smaller caliber. The latter are naturally less in number than in the normal nerve. This is more marked in the dogs experimented on when both branches of the sciatic are cut, than when the internal popliteal alone is cut. The conclusion to be drawn from this is that the disturbance in function of the spinal cord is in proportion to the number of fibers injured and constitutes an unfavorable condition in so far as it concerns the resistance of the neurons to the injury which they have undergone.

It is interesting to note that the authors find that the new fibers, though smaller than those of the uninjured nerve, are as great or greater than before section, and that their number depends largely on the distance above the point of section. They make their enumerations at not less than a centimeter above this point, and frequently as high as fifteen to twenty millimeters.

At the neck of the cicatrix the writers have not counted the fibers, although superficial examination would indicate that the fibers are increased proportionately to the diameter of the cicatrix. In end to end suture the caliber of

the fibers in the cicatrix is apparently the same as in the fibers in the lower or distal portion of the nerve. In the graft the diameters of the fibers are a little larger than in simple sutures.

Sometimes in simple sutures there is a slight edema of variable development, generally in the so-called metamorphic zone; in the graft this edema never appears in the process of the graft itself, but only above and below it.

Condition of the Nerve Below the Cicatrix.—In a general way, in spite of frequent perfect muscular function, there is always notable diminution in the nervous tissue. While the number of fibers is generally increased, their diameter, or caliber is usually less than in the healthy nerve. Regeneration is rapid even in cases of nerve graft. This is true both as to the number of fibers and their caliber. Only functional disturbance is found below the cicatrix.

The age and state of health of the animals experimented on seemed to have no marked influence on nerve regeneration and restoration of muscular function. Even infection at the site of section apparently had no special effect. On the other hand, individual predisposition certainly plays an important part in the proliferation of nerve fibers and neuroglial sheaths. Instances are then cited.

Trophic Disorders.—Trophic ulcerations are not rare. It is a disputed point as to whether these trophic ulcers are the result of injury to the nerves themselves or the secondary result of mechanical disturbances, such as a disturbed gait or other disordered movement resulting from nerve section.

In abstracting the instances where trophic ulcers have exercised an evident influence on muscle restoration, the authors conclude that there generally exists a parallelism between this restoration and regeneration of the nerve; but this parallelism is not absolute and relations between muscle restoration and nerve regeneration are not simple. At the end of four months, gait is usually well restored; at the end of six months there is no apparent defect of motility of any kind. The authors also note that, although in three instances muscle restoration did not keep pace with nerve regeneration, nerve regeneration, nevertheless, showed a distinct relationship to the age of the cicatrix and differed markedly in different animals.

In the final paragraphs the writers sum up the comparative advantages and disadvantages of end to end suture and nerve graft. After a thorough study of their cases, they come to the opinion that end to end suture gives the better results.

JONES, Detroit.

TYPES OF FEEBLEMINDEDNESS IN CHILDREN. TH. GÖTT, Klin. Wchnschr. **1**:2288 (Nov. 11) 1922.

As yet we have reached no uniform classification of feeblemindedness in children. Psychiatric, neurologic, psychologic and other avenues of approach have not made it possible to differentiate between the congenital and acquired forms of this condition. Feeblemindedness may occur in both the physically sound and in those suffering from physical ailments, and Gött has grouped the conditions as follows:

1. Feeblemindedness with evidence of organic brain disease. Naturally all cases of feeblemindedness come under this heading, as it is difficult to imagine such a defect without some organic brain change.

(a) In this group there is evidence of a definite cerebral lesion as in the palsies of childhood, choreo-athetoid conditions and epilepsy. Pathologically

one finds a great variety of cerebral lesions. Even here it is at times difficult to determine if the lesions are prenatal or postnatal. A clearly endogenic form of feeblemindedness is probably represented by tuberous sclerosis in which there are sebaceous tumors of the face, epileptic attacks and tumors of the heart muscle, kidneys and brain. Trauma is one of the chief ectogenic factors, but inflammatory conditions must also be considered. It is evidently useless to attempt an etiologic classification of this disease group.

(b) Here are to be considered cases of feeblemindedness with gross organic brain lesions as evidenced by malformations and deformities such as microcephalus, hydrocephalus, "turmschädel" and agenesis.

(c) The author places here the rather rare familial infantile amaurotic idiots. This condition, as is known, is confined almost entirely to the eastern European Jews.

The degree of feeblemindedness of these organic types is variable and is no index to the location of the lesion or its severity.

2. A second clinical major group of feeblemindedness is distinguished by bodily signs with no definite neurologic findings.

(a) First come the thyrogenous deficiencies, especially the sporadic infantile myxedemas. In this condition both physical and mental spheres may be markedly altered. In other endocrine disturbances mental changes may be associated, but whether these changes are the result of the dysfunction alone or the entire picture, or whether they are based on a pathologic process, is not clear. Brain deformities have been found in myxedemas, so it appears that every mental alteration in this type of case should not be attributed to glandular dysfunction. Undoubtedly the apathy and slowness result from the thyroid disturbance. As therapy is of benefit in this group, the possibility of such a condition being present must be considered in every case of feeblemindedness. In the cretins one may not obtain the desired results with therapy, especially in the older and more severe cases.

(b) Other endocrine disturbances, as adiposity of hypophyseal origin, may be associated with feeblemindedness. Unfortunately glandular therapy is of uncertain value in these cases.

(c) Closely related to the myxedema group in which the pathology is unclear, is the group of mongolian idiots. This condition apparently has a fetal origin, but thus far no internal secretory or pluriglandular cause has been found. As noted by Dollinger, a fairly constant factor is that these children are usually the last born and also born of older parents. Mentally they are quite the opposite from the cretin. They are lively, impulsive and represent a versatile feeblemindedness. They are rarely as severely affected as the myxedematous child.

(d) Syphilitic and rachitic children play a rather small part in this group.

3. Here is considered the group of feeblemindedness in which there are various physical anomalies, all of which are of a minor character, but indicate definite pathologic changes.

4. While the former groups all show some bodily anomaly, this group, on the contrary, is made up of children in which the physical examination is entirely negative. It is rather the rule that these children have developed normally for several years, or probably up to the fourth or fifth year, when rather suddenly mental alterations occur. The speech is impaired or the child even becomes mute, presenting a so-called dementia infantilis or praecocissima, a rather unclear process which has been considered by some as related to dementia praecox.

Formerly a physician was more interested in the physical anomalies than in the feeblemindedness, and it is with this thought in mind that a classification has been attempted. The special interest in feeblemindedness is the question of prognosis. To consider this in an intelligent manner it is necessary to determine where possible the nature of the disease process, as in certain types therapy is available, while in other conditions the disease process appears to be progressive. Much help may be obtained through mental ratings, but this in itself is of little value in determining the character of the disturbance.

MOERSCH, Rochester, Minn.

A CASE OF TRAUMATIC DEMENTIA. R. BENON and G. LEFÉVRE, Rev. neurol. **26**:705 (Sept.) 1919.

The authors comment on the rarity of traumatic dementia, having observed not over ten cases (not all of these definitely established cases) in five thousand patients under their care. They define traumatic dementia as "essentially characterized by a state of partial enfeeblement of the mental faculties, apparently associated with circumscribed lesions, single or multiple, of the brain substance, and different from those observed in general paralysis."

A brief resumé of the case runs as follows: The patient, a man, aged 64, was injured by a fall from a bicycle when 54 (winter of 1908 or 1909); this resulted in cerebral concussion. After the injury he was not able to resume his occupation. There was a very clean-cut lessening of intellectual faculty, but without delirium or asthenia. His emotional reactions were hypoactive; there existed also a generally lowered psychomotor activity. He suffered nervous crises, epileptic in character, and fugues in 1914 and 1919. Later he was committed to an asylum with a diagnosis of partial mental deficiency or weakness of acquired character. He was neither alcoholic nor syphilitic; he had an epileptic son.

More detailed study of the case brings out the following: he was unconscious for forty-eight hours after the injury; on the fifteenth day after the injury he had complete amnesia and attempted to return to work, not even recalling that he had been hurt. He grew progressively worse until at the end of a year he showed incoherent thought, memory defect, and disorientation. His first fugue occurred six years after the injury. From 1914 to 1918 he manifested no interest in the World War, its events, nor the part taken in it by his neighbors. The second fugue occurred in 1919. He was away from home several days, and had no memory for anything he had done or seen during this period. It was learned later that he had slept in unusual places, and had gone forty-eight hours without food.

His epileptic attacks appeared shortly after the original injury, and occurred every ten to fifteen days. They were not unlike grand mal seizures, although he never injured himself in falling. He complained of pain in the head. The attacks lasted from five to fifteen minutes.

The authors then give a detailed account of his mental state as revealed by examination in May and June, 1919. The dementia or mental defect showed itself largely in the fields of memory, attention and judgment. There existed anterograde as well as retrograde amnesia, the former being more marked. His memory for places was better than his memory for dates. Facts acquired in school were better retained than recent experiences. Simple calculations such as $5 \times 8 = 40$, might be done well on one or two tests; "7×9, I cannot tell." "$9 \times 10 = 90$." "9×9, I do not know exactly."

He manifested a tendency to confabulation. He seemed to have some insight into his condition, recognized that his memory was at fault, but ascribed it to old age rather than to his accident. His general emotional reactions were diminished. He apparently took little interest in the whereabouts and fortunes of his family, and his general activity was markedly retarded. He lay in bed from day to day, and allowed himself to be carried or moved rather than exert himself.

His seizures were observed in the hospital. They were not always ushered in by an initial cry. At times he let objects fall which he had been holding in his hand; occasionally he bit his tongue, or had involuntary micturition. The convulsions were more frequently confined to the right side. Sometimes he presented episodic signs of mental confusion. On the days following his attacks, memory disturbances were more marked. He averaged two or three attacks a month. The Babinski sign was frequently present during an attack and sometimes could be elicited for two or three days after the attack.

In summing up the case, the writers think it striking from three points of view: clinical, etiologic, and diagnostic. The clinical picture has been fully presented. A close study apparently ruled out any cause for the mental let down other than the injury. At this time he was neither syphilitic or alcoholic, and later study showed little or no evidence of arteriosclerosis.

The paper concludes with the differential diagnosis between traumatic dementia and post-traumatic chronic asthenia. In the latter, memory is practically intact, although recall may be slow, difficult, and painful. The asthenic is attentive, but fatigues easily. His judgment and reason are normal. This is not true in traumatic dementia. Lumbar puncture is negative in the asthenic; in traumatic dementia there is usually a slight increase in the lymphocytes and in the albumin or globulin.

In a final summary the authors bring out these points: (1) traumatic dementia is rare; (2) cranial traumatism is a determining rather than a fortuitous cause; (3) clinically, the picture is that of an amentia; somatic symptoms including epileptic attacks may be slight or absent; (4) traumatic dementia is dementia of organic type; (5) traumatic dementia has been mistaken for chronic traumatic asthenia, but the two disorders are easily distinguished in the large majority of cases.

JONES, Detroit.

BLINDNESS IN MIGRAINE. WALTHER LÖHLEIN, Deutsch. med. Wchnschr. **48**:1408 (Oct. 20) 1922.

The author reports the case of a man, aged 42, who, on December 21, in the course of a migraine attack became almost totally blind. On examination it was found that there was a large hemorrhage in the vitreous of the right eye which connected with a diffuse hemorrhage in the retina. The disk and surrounding area were covered with blood, but at the periphery of the retina the vessels could be seen. The inferior nasal vein was dilated, tortuous and thrombosed, as was also one of the smaller veins in the region of the macula. The arteries were rather pale, especially those going to the inferior nasal region. The part of the retina which could be distinguished was edematous. There was slight peripheral vision, and reaction to light was feeble.

It was learned that in 1916 the vision had been similarly affected in the left eye during a migraine attack. This eye now reacted only slightly to light. There was an external strabismus, the disk was pale and not well defined. The physiologic cup was obliterated, having been filled in with

grayish-white tissue. The veins were normal in size and the arteries were fine and pale pink. In the region of the disk numerous yellow and white glistening spots were noted. Beyond the ability to count fingers in a small peripheral field, vision was practically gone. With this history and these findings it was apparent that the patient had had a process in 1916 similar to the one now noted in the right eye.

Since the age of twenty years the patient had suffered from severe migraine attacks which were only relieved by morphin. These attacks were associated with frontal and temporal headaches, sensitiveness to noises and smells, paresthesias of one side of the face, thickness of the tongue, gastric distress, later vomiting and ending in sleep; and finally complete recovery. During the attacks, transient blurring of the entire field of vision might occur, and even blindness lasting several hours. It was following such an attack in 1916 that he lost vision in the left eye. The examination at that time showed a large hemorrhage which was gradually absorbed, with slight return of vision.

The history and general examination revealed an otherwise healthy man. The neurologic examination substantiated the diagnosis of migraine and visual disturbance.

The progress of the patient showed absorption of the hemorrhage and a return of central vision to 5/25. Some time later the writer noted a fresh hemorrhage in the region of the inferior nasal vein which naturally made the prognosis very doubtful.

There is no doubt in the writer's mind that the vascular lesions are to be associated with the migraine. The repeated attacks of migraine produce a "locus minoris resistentiae," which ultimately, with recurring attacks, leave a permanent residual. Persistent hemiplegias, hemianopias, aphasias, etc. belong in this group. In some of these cases postmortem examinations have revealed a thrombosis which may have been facilitated by some residual process—the result of repeated vascular spasms. Charcot pointed out that, especially in ophthalmic migraine, the vascular spasm appears to play a very definite part.

The author was able to find two similar cases in the literature, one described by Galezowski in 1882. Braasch and Levinsohn, and Voss have also seen similar hemorrhages. Several writers have observed contraction of the retinal vessels during a migraine attack. Hilbert was able to note, in a case of unilateral migraine, a pallor of the retina and pulsation of the central artery, which under amyl-nitrite entirely disappeared. As analogous processes in the blood vessels during a migraine attack. Hilbert was able to note, in a case of unilateral or hemianopic scotoma, as noted by Pagenstecker and Hensen.

In discussing the possibility of further hemorrhages, the author recalls that he later observed a fresh hemorrhage in the right eye. The migraine attacks he attempted to control by the use of amyl-nitrite and found that the retinal vessels remained dilated for several hours following its use. However, he feels that the amyl-nitrite may not suffice to ward off vascular spasm in an attack lasting several hours.

MOERSCH, Rochester, Minn.

THE INCIDENCE OF THYMIC ENLARGEMENT WITHOUT SYMPTOMS IN INFANTS AND CHILDREN. ROY M. GREENTHAL, Am. J. Dis. Child. **24**:433 (Nov.) 1922.

Greenthal studied two thousand consecutive patients presenting both medical and surgical conditions and ranging in age from 3 days to 12 years.

Of this number only three came with symptoms referable to the thymus gland. The diagnosis of thymic enlargement was made on the basis of physical examination, roentgen-ray examination, and in some instances, postmortem examination.

The recent study of Blackfan and Little is quoted at considerable length. Blackfan and Little established definitely the character of the thymus shadow in roentgen-ray examinations and found, in a series of sixty unselected infants, thymic enlargement in twenty-nine or 48 per cent. In Greenthal's series, physical examination revealed an enlarged thymus in 4.5 per cent. and roentgen-ray examination showed enlargement in 25.6 per cent.: the latter examination was made on 351 patients. The author regards his results as too low and ascribes this to the probable greater age of his patients. In analyzing his results with reference to associated conditions, the author finds the highest incidence of thymic enlargement occurs with congenital defects and malformations. Roentgen-ray or radium emanation treatment is recommended in all cases where thymic enlargement has been demonstrated.

VONDERAHE, Philadelphia.

ENDOCRINE DISTURBANCES AND LATE EPILEPSY. M. PERRIN and G. RICHARD, Rev. neurol. **26**:698 (Sept.) 1919.

This is a rather late abstract but it touches upon a certain type of epilepsy of such importance as to make the abstract timely. The authors report two cases with conclusions that are worthy of more than a passing thought. In the introduction they mention certain rare forms of epilepsy associated with a hypofunction of the parathyroid glands; the relation between certain hysterical conditions and various ovarian disturbances, the relation between certain forms of neurasthenia and testicular troubles. They also refer in the introductory paragraphs to myasthenia gravis and paralysis agitans, as instances of disorders possibly of endocrine origin. They also lay emphasis on the point that a single endocrine gland is rarely disordered alone, but that we are more apt to find pluriglandular disturbances.

Their first case is one in which they think ovarian insufficiency was closely associated with late epileptic attacks. The patient was a woman 38 years old, with a family history negative for nervous and mental diseases. Up to the age of 29 her medical history was unimportant. She was then an intelligent, well balanced, artistic musician. About that time she showed definite symptoms of exophthalmic goiter. Her menstrual periods, hitherto regular and painless, became irregular and painful six months after the first hyperthyroid symptoms; three months later she suffered her first epileptic attack at a time when the menses were due. After that, each time the menses failed to appear she suffered an epileptic attack; there was always some relation between the epileptic attack and menstrual disturbance.

When first seen in the hospital ward at the age of 38, she was emaciated and showed definite mental disturbance, being completely demented. The blood Wassermann reaction was negative. Later studies showed definite involvement of both the pituitary and the suprarenal glands. In this state the patient contracted influenza and died three days later of bronchopneumonia and cardiac insufficiency. A resumé of the case reveals the following sequence: exophthalmic goiter; menstrual irregularities (ovarian disturbances); epileptiform attacks; pituitary, and finally suprarenal dysfunction.

The second case was in a woman, aged 20, whose family history for nervous and mental diseases was negative. The personal history revealed that the patient did not develop normally. She learned to talk later than the average, had tantrums as a child, was difficult to manage, and exhibited bizarre memory defects. At the age of thirteen she had her first epileptic attack, generalized in character, which seems to have been precipitated by seeing the sudden death of a man who was killed in falling from a ladder. Two months after this incident, the patient had her first menstrual period. From that time on, there was an apparently close relationship between the menses and the epileptic attacks. The patient attended clinic after clinic, with little relief, except when under bromids; even then she always had seizures shortly before or during the menstrual period. Mentally, she deteriorated until she lost all interest in her environment. When first seen she showed marked hebetude; the muscles were soft and flabby; the countenance was pale, the eyes without expression, the mouth open, the tongue hanging out and swollen; the eyebrows were scanty, the hair abundant. The thyroid gland was atrophied, and the patient complained of being susceptible to the cold weather of Switzerland.

As long as bromids were given she had but one attack a month. From September, 1916, to February, 1917, she was closely observed, and it was noted that the epileptic attacks were closely associated with the menses. Under treatment with thyroid and ovarian extract (later ovarian extract alone), the bromids being discontinued, the patient showed marked improvement. Unfortunately she died of bronchopneumonia following influenza.

The authors failed to get a necropsy in either case, but base the close relation between the epileptic seizures and the endocrine disturbances on clinical grounds.

The remainder of the paper deals with the literature on the subject. The conclusions are that some cases do well on glandular extracts alone; others do better on a combination of the extracts and the bromids. It is the opinion of the authors that too much emphasis should not be laid on the results in two cases, and that the subject calls for further study and comparisons.

JONES, Detroit.

SENILE GENERAL PARALYSIS. RISER and GAY, Encéphale **18**:35 and 101 (Jan. and Feb.) 1923.

It is usual to regard the fourth and fifth decades as the time for the appearance of general paralysis. Juvenile forms are well-known, but the possibility of general paralysis appearing after the sixties is little recognized. Cestan has described in detail the clinical picture of the disease as it appears in later life. Statistics from various countries and numerous writers show only one thing in common—the relative rarity of a senile form of general paralysis. Statistics published prior to the development of the serology of syphilis must be discounted. But, in general, one might accept an estimate that from one to two per cent. of general paralysis occurs in the sixth or later decades.

The authors insist that the pathologic anatomy in the senile and ordinary forms of general paralysis is the same, but that in the senile form there may be supplementary lesions—diffuse sclerosis, and arteriosclerotic vascular lesions —which may complicate the clinical picture. The diffuse sclerosis will account

for symptoms suggesting senile dementia. To establish a diagnosis, the serology must be typical of general paralysis. Among the physical signs, pupillary changes alone are of much value. Psychic changes are in no way pathonogmonic and from the psychologic aspect alone it may be impossible to differentiate between general paralysis and senile dementia. As for the serologic picture, one feature is of importance—it is extremely resistant to change by antisyphilitic treatment.

The differential diagnosis of senile general paralysis may be easy or difficult. As a rule it is easily distinguished from cerebral arteriosclerosis, the dementia following repeated cerebral vascular accidents, and the dementia from lead poisoning, chronic alcoholism or epilepsy. Senile dementia too, is usually not to be confused with senile general paralysis. When meningeal syphilis, late syphilis, cerebrospinal syphilis with alcoholism, and a delayed, gradually progressive cerebral syphilis with remissions, have to be considered, differential diagnosis may be difficult.

HYSLOP, New York.

THE INCIDENCE OF MENINGITIS IN EARLY INFANCY, WITH A DESCRIPTION OF TWO CASES DUE TO UNUSUAL ORGANISMS.

J. V. COOKE AND HOWARD H. BELL, Am. J. Dis. Child. **24**:387 (Nov.) 1922.

The cases of acute meningitis studied by Cooke and Bell occurred in infants under the age of 3 months: four cases were due to meningococcus, two to streptococcus, two to pneumococcus, two to organisms related to the colon bacillus. The two last cases and their associated organisms were studied in detail. In one instance the organism belonged to the group of paracolon bacilli. In the other instance the organism isolated was an encapsulated, proteolytic, nonfermenting bacillus which apparently has not been previously described. This organism presents a tough elastic growth on culture mediums and the authors have suggested *Bacterium elasticum* as a suitable name. It is noted by the authors that in the last two cases of meningitis, because of the characteristics of the bacteria and the absence of recognizable infection elsewhere, the bacteria gain entrance through the intestine. To explain the occurrence in early infancy, the hypothesis is advanced that there is an increased permeability of the intestinal mucosa to bacteria because of: (1) absence of inherited immunity to the colon group; (2) imperfect power of antibody formation in young infants; and (3) the general lowered resistance accompanying malnutrition.

VONDERAHE, Philadelphia.

INTRAVENTRICULAR AND SUBDURAL SERUM TREATMENT OF MENINGOCOCCUS MENINGITIS IN INFANCY.

W. W. HOWELL and S. A. COHEN, Am. J. Dis. Child. **24**:427 (Nov.) 1922.

The authors noted that in hospital cases of meningococcic meningitis, a comparison of results in a series of cases treated by lumbar puncture without serum did not differ materially from a series treated with serum. The reasons advanced for this observation are: (1) delayed treatment before entering hospital; (2) failure of serum to reach the focus of inflammation. This latter condition results, the authors state, from interference with the flow of cerebrospinal fluid because of inflammatory products at the base of the brain and the frequent closure of the foramina of Luschka and Magendie, with associated internal hydrocephalus. In consideration of this the authors recom-

mend introducing antimeningococcic serum into the ventricles and the subdural space after withdrawal of fluid by lumbar and ventricular puncture. The technic of the methods are described; they are intended, of course, only for infants. In thirty-six patients treated by these methods, there was a mortality of 57.7 per cent. as compared with a mortality of 62 per cent. in a group of generally more favorable cases treated intraspinally.

VONDERAHE, Philadelphia.

ACUTE MANIC-DEPRESSIVE INSANITY (ACUTE MANIA) CURED BY THYROIDECTOMY. A. STOCKER, Rev. neurol. **26**:711 (Sept.) 1919.

The author makes a dozen or more references to the literature on the effect of surgical procedures in psychoses associated with thyroid disturbances. Most of these references are to cases with either manic or depressive psychoses.

The case reported, from the neurologic clinic of Jassy, was that of a woman, aged 18. Her family history was negative for nervous and mental diseases and for syphilis. Physical and neurologic examinations were practically negative with the following exceptions: noticeable exophthalmos; pulsation in the neck over the region of the thyroid gland; and general emaciation. Mental examination revealed: general restlessness and increased psychomotor activity; mildly elated mood and a tendency to identify herself with important personages; laughter and distractibility; pressure of speech; perseverâtion; mild erotic tendency; playfulness; and meddlesomeness. Simple calculations were fairly well done, but there was difficulty in concentration. Such was her condition on admission about March 20, 1918. May 7, an operation was performed. She quieted down almost immediately, and twelve days later was discharged as cured.

May 31, of the same year, she was examined again. At this time she cooperated well; recalled her previous manic state; recognized errors in her calculations and corrected them without mistake, but with evident astonishment over her inaccuracies while in the manic state.

Histopathologic examination of the thyroid gland revealed in general: the evidences of functional overactivity; "active" epithelium (elongated cells with enlarged nuclei); diffuse colloidal substance overspreading the walls of the follicles, and proliferation of the vessels.

The writer thinks that the result obtained by operation owes its efficacy and rapidity of action to the fact that the patient presented a frank, acute manic state. He believes that cases like this, with absence of delirium and ovarian disturbance, offer a good prognosis with operation. Moreover, cases like this when treated early are less apt to show dysfunction in other glands of internal secretion.

JONES, Detroit.

STUDIES OF SCHIZOPHRENIC REACTIONS. G. W. HALL AND CLARENCE A. NEYMAN, J. Nerv. & Ment. Dis. **56**:433 (Nov.) 1922.

The authors made very complete physical and laboratory examinations of fifty patients showing schizophrenic reactions. In one patient, aged twenty-one, examination showed a slightly hypertrophied heart, second aortic sound accentuated, blood pressure 174 systolic and 122 diastolic, generally increased non-protein nitrogen constituents in the blood, a basal metabolism increased

14 per cent. and an urea output in twenty-four hours of 3.6 gm. A diagnosis of chronic interstitial nephritis was made and the patient was put to bed on a nephritic diet until the constituents of the blood became normal and the basal metabolism decreased to plus 1 per cent. A second case showed a slightly positive pilocarpin reaction and a high sugar tolerance with an increase in weight of 150 pounds (68 kg.) in the course of a year; a diagnosis of pituitary disturbance was made. A third case gave clinical and laboratory evidence of hyperthyroidism and nephritis. In the final case described, nothing abnormal was found on physical or laboratory examination, but psychanalysis revealed an inferiority feeling and much sexual coloring.

These cases are cited as examples of a suggested grouping into toxic, endocrine, and psychogenic schizophrenia. The authors avoid the use of the term "dementia praecox" because they believe it represents "a clinical syndrome, not a disease entity."

VONDERAHE, Philadelphia.

THE REGIONS OF THE CEREBRO-SPINAL SYSTEM IN WHICH THERAPEUTIC INJECTIONS SHOULD BE DONE. H. C. SOLOMON, Ann. de méd. **13**:57 (Jan.) 1923.

Solomon reports experiments based on the injection of measured quantities of neutral phenolsulphonephthalein in the lumbar subarachnoid space, the cisterna magna and the cerebral lateral ventricles; with a study of the amount of the dye in the spinal fluid obtained by a second puncture at one of the sites other than the one where the first injection was made. A highly important feature demonstrated is that the spinal fluid content of one of these regions can be drawn to one of the other spaces, either by aspiration or by the augmentation of pressure determined by addition of saline. The experiments in total suggest that the displacement of the dye in subarachnoid spaces is the result of diffusion and not of a true spinal fluid circulation.

Regarding sites for therapeutic injections, the following conclusions are reached:

1. In strictly lumbar lesions, injection in the lumbar arachnoid culdesac is justified. When the pathologic process is dorsal or cervical, cisterna puncture should be made at the same time as, or shortly after, the lumbar injection.

2. In processes affecting the base of the brain, whether syphilitic lesions of the cranial nerves, a syphilitic or tuberculous basilar meningitis, or an optic neuritis complicating tabes, the injections should be made in the cisterna so that the therapeutic agent reaches directly the base of the cerebrum.

3. When the lesions are cerebral, cortical or otherwise (not basilar), the injections should be in the subarachnoid spaces of the encephalon or into the cerebral ventricles.

4. When the encephalon and spinal cord share alike in the pathology, the injection of the therapeutic agent should be in the ventricles with a secondary aspiration at the lumbar site or vice versa.

5. Where meningeal adhesions prevent the free diffusion of the spinal fluid, therapeutic injections at all of the several sites are indicated.

DAVIS, New York.

STUDIES IN EXHAUSTION: IV. PHYSICAL TRAUMA. G. W. CRILE, Arch. Surg. **6**:489 (March) 1923.

Crile and his associates have studied the conditions producing exhaustion or shock from various angles. In their first three papers they considered the

effects on the economy of extreme degrees of normal consciousness, insomnia, exertion, and emotion. In the present paper the effect of exhaustion due to pathologic conditions is studied.

Physical trauma produces shock as proved by blood pressure readings, the degree of shock varying directly with the amount of tissue injured, with the intensity of the injuring stimulus, and with the number of injuring impacts. The degree of shock produced by physical trauma varies inversely with the phylogenetic protection of the injured tissues; the injury of tissues that have been protected throughout the evolution of the organism, as the brain or lungs, produces but little shock as compared to the injury of such exposed regions as the abdomen, skin and extremities. Injury of the deep, protected tissues produces collapse rather than shock. It was found that the degree of shock varied directly with the nerve supply of the injured tissue, that blocking the nerve supply of that tissue would prevent the shock otherwise caused by an injury. Exhaustion of the vasomotor mechanism is present in shock but is not the only factor in its production. A state of shock produced by abdominal trauma has no notable effect on the blood count. In shock the nerve cells in the brain and cerebellum show physical changes and react differently to various stains. In a series of animals in which the spinal cord had been completely severed, no amount of trauma of the distal parts of the body caused the subjective symptoms of shock or physical changes in the brain cells. Transfusion of blood by direct methods from a shocked to a normal dog did not cause the development of symptoms of shock in the second dog. Hence shock is not due to the presence of toxic substances in the blood. In all these experiments, one of the most constant and striking features was the fact that the condition of shock was always accompanied by histologic changes in the cells of the central nervous system. The essential cause of exhaustion from physical trauma is identical with that of exhaustion from insomnia, by emotion and by exertion, as presented in the preceding studies in this series.

GRANT, Philadelphia.

SYNDROME OF SUBACUTE DEGENERATION OF THE LONG FIBERS OF THE LATERAL MOTOR BUNDLES. ALFRED GORDON, Rev. neurol. **28**:969 (Sept.-Oct.) 1921.

The author reports two cases. The earlier paragraphs refer to cases with or without anemia. The clinical picture usually shows: progressive paralysis of the lower extremities, and in advanced cases, of the upper extremities; ataxic phenomena; characteristic sensory disturbances (paresthesia and analgesia, and change from spasticity to flaccidity with preservation of the toe phenomenon). Variations in the chronology and intensity of these symptoms may occur. As noted above anemia may or may not be present.

The two cases which the author reports show definite involvement of the motor columns. They are analogous to cases of lateral sclerosis reported in the literature except that they do not begin or continue as a disseminated myelitis or sclerosis. While they present all the evidence of a sclerosis of the pyramidal tracts yet they differ from classical spastic paraplegia. The course of the symptoms indicates that large portions of the motor tracts are intact by virtue of the absence of rigidity. Nevertheless, the lesion is sufficiently irritative to produce exaggerated tendon reflexes, ankle clonus, and the plantar reflex characteristic of subacute degeneration of the posterior and posterolateral columns. Hence the title of the paper. He thinks it justifiable

to consider three varieties of involvement of the long fibers: (a) posterior, (b) posterolateral, and (c) lateral alone. He thinks his two cases illustrate involvement of the long fibers of the lateral motor portion of the cord.

JONES, Detroit.

THE COLLOIDAL GOLD REACTION IN ACUTE POLIOMYELITIS. J. C. REGAN, A. LITVAK, and C. REGAN, Am. J. Dis. Child. **25**:76 (Jan.) 1923.

The cerebrospinal fluids in forty-two cases of acute poliomyelitis were studied with reference to the colloidal gold reaction. In every instance a reaction was obtained in the so-called syphilitic zone, a characteristic reading during the first and second week being 11½22100000. In the cases where the reaction extended to the seventh dilution the patient presented marked polyneuritic or meningitic symptoms or pronounced paralysis. The curves showed similar characteristics during the first and second weeks of the disease and thereafter gradually declined; 65 per cent. were normal at the eighth week. Cases in which a normal reduction occurred early were mild types. In the fatal cases the reactions were not distinctive, so that while the test is of particular value in diagnosis it affords no information as to prognosis. There was no constant ratio between the number of cells per cubic millimeter and the reaction; the gold curve tended to remain elevated after the cell count had become normal. It is worthy of particular note that the authors could trace no relationship in a positive reaction to the presence or absence of globulin. The study is concluded with a consideration of the differential diagnosis of other conditions which present a similar reaction.

VONDERAHE, Philadelphia.

ALTERATIONS IN THE CURRENTS AND ABSORPTION OF CEREBROSPINAL FLUID FOLLOWING SALT ADMINISTRATION. F. E. B. FOLEY, Arch. Surg. **6**:587 (March) 1923.

An attempt is made to explain the effect of raising the hypertonicity of the blood on the production and absorption of the cerebrospinal fluid. An increase in the tonicity of the blood may be produced by the direct injection into the blood-stream or into an exposed loop of intestine of an hypertonic 30 per cent. solution of sodium chlorid. Following this rise in the tonicity of the blood, a marked fall in the spinal fluid pressure occurs as shown by a manometer connected to a spinal puncture needle. The greater the increase in the tonicity of the blood, the greater the fall in the spinal and intracranial pressure. The cause for this fall in intracranial pressure seems to be a profound disturbance in the mechanism of the cerebrospinal fluid absorption rather than to a decrease in brain bulk and enlargement of the cerebrospinal spaces. A new ratio is established between cerebrospinal fluid production and absorption pressures. As the hypertonicity of the blood increases, intraventricular absorption of the cerebrospinal fluid through the choroid plexus and ependyma occurs. The fluid is absorbed through the capillaries of the brain substance with reversal of fluid flow in the perivascular sheaths. More fluid is absorbed along the sheaths of the cranial and spinal nerves. Apparently direct absorption occurs into the vessels traversing the subarachnoid space. As these increases in the points in which absorption takes place are brought about, alterations in the gross currents of the fluid result. The most striking of these is a reversal of flow which may be demonstrated in the aqueduct and ventricular system.

GRANT, Philadelphia.

ON BILATERAL EFFECTS FROM THE UNILATERAL SECTION OF BRANCHES OF THE NERVUS TRIGEMINUS IN THE ALBINO RAT. KENJI NITTONO, J. Comp. Neurol. **35**:133, 1923.

The purpose of this investigation was to observe the sequence of changes on the side of operation in degeneration and regeneration following section of the trigeminus and its branches, and also to determine whether there were any corresponding changes in the trigeminal ganglion or branches on the intact side of the operated animals. The observations of the first group conform in general to the classical descriptions; those of the second group are of more special interest.

On the intact side of the operated animals there were found changes of the same type as on the operated side, though fewer elements were involved. Measurements were made of changes in diameter of nerve cells and nerve fibers consequent on the lesions on both operated and intact sides. The changes on the two sides were not exactly alike, yet they were similar. It is suggested that specific neurotoxins or neurolysins, formed on the side of the lesion, are responsible for the changes observed on the intact side.

HERRICK, Chicago.

SOME ASPECTS OF ANIMAL MECHANISM. SIR CHARLES S. SHERRINGTON, Ment. Hyg. **7**:1 (Jan.) 1923.

The reader who likes closely knit reasoning always is sure of finding it in Sherrington's articles. This address before the British Association for the Advancement of Science reaches out toward a philosophic discussion, but retracts to the physiologic problems in which the author is at home. Is life the running of a machine? How does it work?

The complicated harmonies of posture as provided by purely reflex action are discussed. A second topic is the regrowth of nerve fibers after section, with emphasis on the overlooked influences of the contact of neighboring cells on each other's destiny, rather than on the influence of future function. The topic is expanded with illustrations from fetal life paralleling those of regenerating nerve.

What is mind? Or is there a mind? Evidently "in the mental parts of the brain there is nothing but the same old structural elements." Mental and nervous actions have in common: fatigue, habit phenomena and memory (the reflex engram); the likenesses grow as we learn more. But there is no doubt of the unity of the animal, of the man; can we conceive a unity that is part mechanical and part not? Sherrington does not answer beyond an inference, but restates the problem. A biologic process is constructing a social organism in man which is "broadly speaking, his alone—namely, a mind actuated by instincts, but instrumented with reason."

BOND, Philadelphia.

STUDY IN BASAL METABOLISM IN DEMENTIA PRAECOX AND MANIC DEPRESSIVE PSYCHOSIS. CHARLES E. GIBBS and DOROTHEA LEMCKE, Arch. Int. Med. **31**:102 (Jan.) 1923.

The authors studied the basal metabolism in thirty-one cases of dementia praecox, manic-depressive psychosis and psychoneurosis. The cases were selected as far as possible with essentially negative symptomatology of endocrine disorder. The depressive group tended to give readings below normal; the mixed and manic group gave variable readings; the dementia praecox group

gave variable abnormal readings generally greatly below normal; the psychoneurotic group gave variable abnormal readings. In two cases of manic-depressive depression, thyroid by mouth raised the rate to normal; it failed in another case; in none of the cases did immediate mental improvement follow administration of thyroid. The variations from the normal rate were greater in dementia praecox than in manic depressive psychosis or in psychoneurosis. The authors emphasize the necessity of taking into consideration not merely the clinical group, but the symptoms presented by the individual patient at the time the metabolic rate is determined.

VONDERAHE, Philadelphia.

THE PILOMOTOR CENTERS AND THE PILOMOTOR PATHWAYS. ANDRÉ THOMAS, Rev. neurol. **28**:950 (Sept.-Oct.) 1921.

A preliminary note refers to the studies of André Thomas on the pilomotor reflexes. The text of the article proper is simply explanatory of a plate in colors prepared by Mme. Dejerine which illustrates in a summary way the studies of Thomas. The chart is printed for the assistance of workers in this field. It will enable neurologists to supplement their studies of sensory disturbances due to spinal lesions with observations on the encephalic and spinal reflexes in cases of spinal injury or disease. The plate or chart is printed preliminary to the publication of Thomas' larger work on the pilomotor reflexes, and serves as an aid to those who desire to fill out the clinical elements in the diagnostic topography of cord lesions.

JONES, Detroit.

REFLEXES OF SPINAL FROGS AS INDUCED BY CHEMICAL STIMULATION. JAMES O. FOLEY, J. Comp. Neurol. **35**:15, 1922.

Working on cutaneous reflexes of pithed frogs, it is concluded that the time of reaction to chemical solutions is not due principally to direct mechanical or chemical stimulation as such. The threshold of stimulation by acids indicates that they rank in the following order: sulphuric (N/600), hydrochloric (N/100), acetic (N/40). Stimulation by alkalis indicates rank in the order: potassium hydroxid (N/600), sodium hydroxid (N/100), potassium carbonate and sodium carbonate (N/10). The direct stimulating effect of both acids and bases is apparently due to the degree of ionic dissociation in solution.

HERRICK, Chicago.

TYPES OF CEREBRO-SPINAL SYPHILIS IN CHINA. ANDREW H. WOODS, China M. J. **36**:3 (May) 1922.

After a year's experience, Woods finds that the incidence of nervous syphilis in China is about the same as in Europe and America and that the manifestations do not vary greatly from those seen in other parts of the world.

VONDERAHE, Philadelphia.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, April 19, 1923.

F. K. Hallock, M.D., *President, in the Chair*

THE SPINAL FLUID OF ENCEPHALITIS LETHARGICA.

Dr. J. B. Ayer and Miss J. E. Cockrill.

Judging by the frequency with which the diagnosis of encephalitis has recently been considered in connection with differential diagnosis, a recrudescence of this disease seems imminent. In that, in our experience, the spinal fluid findings have proved of considerable value, and in that our findings are similar to those published previously from our clinic by Foster (J. A. M. A. **77**:365, 1921), it seems best to give them at the present time.

During the past year we have examined fluids from twenty-three patients with encephalitis, the diagnosis resting on the clinical course of the disease and in two instances being checked by necropsy. The findings are shown in table 1:

Table 1.—*Spinal Fluid Findings in Twenty-three Personal Cases of Epidemic Encephalitis*

Case No.	Age	Time Since Onset	Pressure in Mm. of Water	Cells in 1 c. mm.	Globulin (Ross-Jones)	Total Protein Mg. per 100 C.c.	Colloidal Gold	Sugar, Percentage	Wassermann
1	24	3 days	185	0	Present	33	0000000000	0.0576	Negative
2	74	Few days	216	116	None	47	0001221000	0.0727	Negative
3	33	1 week	168	15	Slight	48	0000000000	0.0917	Negative
4	16	1½ weeks	140	4	None	29	0000000000	0.0928	Negative
5	30	2 weeks	150	30	Slight	67	0000000000	0.0689	Negaitve
		2½ weeks	100	12	None	58	0000000000	0.0600	Negative
6	20	2½ weeks	60	0	None	36	0000000000	0.0701	Negative
		3 weeks	120	2	Slight	52	0000000000	0.0700	Negative
7	27	2½ weeks	100	1	Slight	60	1333320000	0.0730	Negative
8	20	3 weeks	180	4	Present	50	0000000000	0.0720	Negative
9	43	3 weeks	...	4	Present	47	0000000000	0.0730	Negative
10	35	3 weeks	150	7	None	37	0000000000	0.0980	Negative
11	51	3 weeks	130	2	None	33	0000000000	0.0740	Negative
12	30	3 weeks	...	4	Present	67	.....	0.103	Negative
13	38	3 weeks	175	1	None	35	0000000000	0.0719	Negative
14	36	3½ weeks	145	34	None	41	0000000000	0.0724	Negative
15	28	4 weeks	50	34	Present	54	0000000000	0.0707	Negative
16	26	4 weeks	...	32	Present	51	0000000000	0.0724	Negative
17	28	5 weeks	115	7	Present	48	0000000000	0.0645	Negative
18	36	2 mos.	140	2	None	33	0000000000	0.0645	Negative
19	26	2½ mos.	50	44	None	40	0000000000	0.0740	Negative
20	20	3 mos.	180	5	Slight	67	0000000000	0.0500	Negative
21	19	21 mos.	250	3	Slight	55	0123321000	0.0606	Negative
22	23	3 years	120	2	None	45	0000000000	0.0625	Negative
23	33	4 years	35	2	None	50	1112321000	0.0657	Negative

It is obvious at a glance that no great change, certainly no change in the fluid which may be called pathognomonic, is found in any of these cases. But when the abnormal findings are grouped, certain changes, which are more or less constant, stand out, on which we believe some reliance may be placed. For

convenience are added in the table our own previous cases and those of Eskuchen (*Zeitschrift für die gesamte Neurologie und Psychiatrie* **76**:568, 1922) and Coope (*Quarterly Journal of Medicine* **15**:1, 1921).

TABLE 2.—*Spinal Fluid Findings in Eighty-Five Cases of Epidemic Encephalitis from the Literature*

	No. of Cases	Pleocytosis (Over 5 per C. Mm.) per Cent.	Total Protein (Over 40 Mg.) per Cent.	Globulin, per Cent.	Colloidal Gold Reaction, per Cent.	Sugar Increase, per Cent.
This series	23	39	74	52.0	17	91.0
Foster, 1921	11	100	91	....	100	91.0
Eskuchen (under 2 mos. duration)	40	60	..	72.7	85	82.5
Coope	11	...	..	....	...	82.0

It is evident from these tables that the fluid characteristic of encephalitis is a clear, colorless fluid, obtained under normal pressure, showing usually slight increase in total protein and a trace of globulin, with frequently a pleocytosis, usually not high, rarely over 100 cells per c. mm., all of the cells being mononuclear. There may also be a colloidal gold reaction, most often in the so-called "syphilitic zone." But the most significant finding is a high sugar reading. These findings are in agreement with a number of writers, and with others we believe them of value in the differentiation of encephalitis from a number of conditions presenting a similar clinical picture.

Perhaps the disease most frequently confused with encephalitis, especially in the early stage, is tuberculous meningitis. In this disease the cells are almost always greatly in excess of the number found in encephalitis, and polymorphonuclear leukocytes are not uncommonly found. The total protein also is greater in amount. Perhaps the most significant difference is in the sugar content, being regularly decreased in tuberculous meningitis, as in fact it appears to be decreased in all forms of meningitis. The accompanying Table 3, covering all of the cases of tuberculous meningitis which have come to us during the past year illustrates this point:

TABLE 3.—*Spinal Fluid Findings in Tuberculous Meningitis*

Case	Cells	Total Protein	Gold Chlorid	Sugar
1	230	118	0001331000	0.0321
2	325	500	0000455442	0.0100
3	200	100	0000444210	0.0400
4	310	77	1123455210	0.0250
5	150	160	0002222200	0.0410
6	485	400	0000000000	0.0864
7	62	138	0000000000	0.0006
8	208	235	0012333110	0.0010
	202	226	0000122100	0.0010
9	106	500	0001122222	0.0010
10	119	190	0000000000	0.0009
11	210	400	0012333210	0.0350

In syphilis of the nervous system of the type which may be confused with encephalitis, the Wassermann reaction is usually present. Also the total protein is commonly greater and the globulin reaction stronger, and in many cases the cells are more numerous. In multiple sclerosis in the progressive stage, the type which may be confused with encephalitis, it has been our experience to obtain strong colloidal gold curves, frequently in the "paretic zone."

We believe that encephalitis usually gives an abnormal fluid which, while not presenting pathognomonic features, is quite different from that found in tuberculous meningitis, and other forms of meningitis, and that it is usually unlike that of the types of syphilis and multiple sclerosis which clinically resemble encephalitis.

DISCUSSION

DR. M. D. ORDWAY: How does the spinal fluid in acute chorea compare with acute encephalitis?

DR. AYER: I remember only one case that we have had, and we thought that was encephalitis. Is chorea encephalitis?

DR. D. J. MAC PHERSON: With regard to Dr. Ayer's question of sugar: we had one crucial case at the Brigham Hospital, in a woman in late middle life who presented a clinical picture suggesting either tuberculous meningitis or encephalitis lethargica. The sugar in the spinal fluid, by quantitative tests done at the Boston Psychopathic Hospital, was reported as above normal. Because of this the diagnosis of encephalitis was considered more probable. At necropsy she proved to have tuberculous meningitis. Increased sugar in the spinal fluid, though suggestive, should not be accepted as an absolute criterion of encephalitis.

DR. PERCIVAL BAILEY: I should like to ask Dr. Ayer to state a little more definitely about the type of gold test. Will he quote figures? I will describe briefly a case that came into the Peter Bent Brigham Hospital. The patient had become rather dull and unable to do his work as a mechanic in an automobile factory. The diagnosis was brain tumor. We made a diagnosis at the hospital of general paralysis. He was sent in for lumbar puncture; the Wassermann reaction was feebly positive, the colloidal gold test typical of general paralysis. He remained in the hospital, was given antisyphilitic treatment without effect, continued to develop meningeal symptoms, and grew increasingly more sick; we thought he might have tuberculous meningitis. There were 145 lymphocytes in the fluid. It was thought by some that he might have encephalitis lethargica. Spinal fluid was taken again and this time there were 386 lymphocytes, the sugar was normal, and the Wassermann reaction was negative. This time we got a meningitic gold curve. The diagnosis was decidedly dubious. The patient died. He never had fever in the whole course of the disease. At necropsy there was found what looked to be a perfectly definite tuberculous meningitis, but microscopic examination proved it to be a case of torula histolytica. The torulae had been counted as lymphocytes in the spinal fluid. It taught me a lesson, namely: to make a histologic examination of every spinal fluid having over a hundred cells.

DR. AYER: With reference to the colloidal gold tests. All except one was in the so-called syphilitic zone. Others have reported general paralytic zone reactions. In the previous series of eleven cases, the fluid findings were similar to the present, so I think there is some value in puting them together. It is interesting that the blood sugar was normal. We had one syphilitic meningitis with more than 500 cells, with sugar below normal. It seems as if there was something about the meningitis that causes sugar to drop, whatever be the cause. I don't wish to be considered an extremist on making a diagnosis on the spinal fluid findings, but I do believe the spinal fluid should have a place in the consideration of the diseases mentioned; if one does not try to read too much into the examination, I think one may get benefit from it.

A SECOND CASE OF ASCENDING COMPRESSION MYELITIS ASSOCIATED WITH UNUSUAL PATHOLOGY.

Dr. Harold I. Gosline and Dr. Owen L. Murphy.

The first case was originally presented by Drs. Weatherby and Gosline in the *Journal of Nervous and Mental Diseases* **51**:242, March, 1920. That patient, following a fall, had pain in the left thigh which spread over his back. Two days later the left leg became paralyzed and the following day, the right leg. There was retention of urine and feces. On the afternoon of the third day, there was anesthesia over the left upper abdomen to the level of the ninth thoracic nerve root. Complete flaccid paralysis of both legs was found together with absent reflexes. Two days later (fifth day) there was total anesthesia to a line corresponding to the seventh thoracic nerve root. Above was hyperesthesia corresponding to the fifth and sixth thoracic roots. Flaccid paralysis existed from the waist down and plantar stimulation caused flexion, then extension, then a momentary spasm of all the muscles of the thigh.

The second case had a long course of thirteen years of chronic respiratory infection following pneumonia. He developed influenza in March, 1923, and appeared to have recovered when he suddenly complained of urinary retention, constipation, and severe pain. The same day the body was hyperesthetic below a line drawn between the sixth costochondral junction and the seventh thoracic vertebra. Knee jerks were sluggish and he had to be catheterized. The next day there was bilateral flaccid paralysis, complete anesthesia with a belt-like area of hyperesthesia above.

In the first case there was a massive fibrinopurulent membrane over the left lower lobe which had broken into the spinal canal epidurally by direct extension. In the second case a similar exudate existed, though no connection with the body cavities could be demonstrated. The appearance of the tissues and the relation of influenza bring up the question as to whether the causative agent of influenza may not injure other tissues as well as the lung, thus allowing invasion of these other tissues, as well as the lung, by secondary organisms.

The second case was one of mental disease. There is considerable evidence that the mental disease in this case may have been related somehow to the chronic infection in his respiratory tract.

DISCUSSION

Dr. J. B. Ayer: Can you elucidate the problem a little? What was the organism that you found?

Dr. Gosline: In the first case it was not cultivated. In the second, it was a pneumococcus. Influenza may harm other tissues and subsequently allow invasion of other parts of the body. From the neurologic standpoint, the exudate gradually compresses the cord and produces symptoms in the usual way.

Dr. J. B. Ayer: There are three points of especial interest to me in connection with Dr. Gosline's cases. The first point concerns the origin of the pus found extradurally. Apparently in these two cases the invasion of the epidural space was from the lungs. On looking up the subject some years ago I found the focus was usually in the vertebrae. Dr. Viets and I reported a case in which the primary focus was in the breast.

The second point of interest is the considerable period during which infection may remain in the epidural space without passing to the subarachnoid

space. In these cases a few days only seem to have elapsed before the organisms passed through the dura. In one case of mine, the fluid was sterile at necropsy in which cord compression by pus must have been present for nine days; another case was sterile four days from the onset of cord symptoms, and meningitis was delayed many weeks thereafter. The two cases referred to were infections with staphylococcus aureus.

The third point, most important from the point of view of prognosis, is this: How much of the paralysis is due to compression from the epidural exudate, and how much is due to myelitic degeneration? In one of the cases referred to, the cord was diffluent at the level of compression after nine days; in the other, although operation was promptly undertaken at Dr. Taylor's inistence on the fourth day of symptoms, release of pus resulted in no benefit. It is therefore likely that, while organisms do not readily pass through the dura, toxins do, and that epidural abscess causes transverse myelitis both by compression and by setting up a true toxic myelitis. These findings are of great interest in connection with the experimental work of Orr and Rows.

Dr. James V. May read parts of a translation of an article by Dr. Karl Wilmanns entitled, "Die Schizophrenie," published in *Zeitschrift für die gesamte Neurologie und Psychiatrie* **78**: Nos. 4 and 5.

IN MEMORIAM

We, the members of the Boston Society of Psychiatry and Neurology, assembled in regular meeting, lament the sudden removal by death of Dr. Herbert Burr Howard on March 6, 1923, and with unwonted sadness we feel his absence from the accustomed place amongst us.

Our deepest sympathy reaches out to the sorrowing family in their loneliness: With them we cherish the memory and achievements of his noble life, and with the community and the state we realize the irreparable loss sustained by the public service which he honored.

Dr. Howard's connection with this society dates back to the early days. He served as its honored president and we are proud of his services, as physician, as hospital superintendent and in the many positions of honor that he filled and especially for his many activities in relation to matters for which this society stands.

We realize that throughout his career, dealing mostly with general hospital problems, he was voluntarily concerned in all matters relating to the mentally ill, and rendered invaluable and pioneer service in framing the laws and in the upbuilding of institutions for their care.

He filled the important positions of superintendent of the State Infirmary, the Massachusetts General Hospital and the Peter Bent Brigham Hospital, which he planned.

He was an influential member and for a number of years chairman of the State Board of Insanity, chairman of the Board of Trustees of the Gardner State Colony, president of the National Hospital Association and chairman of the Hospital Section of the American Medical Association. He held membership in various medical societies.

Through the many years we have felt the influence of his ideals, the warmth of his fellowship, the wisdom of his counsel and the depth of his interest in psychiatry. The members of this society, many of whom are no longer with us, were his most intimate friends and have prized his friendship, the honesty

and strength of his convictions and his rugged good humor along with the refining qualities of his kindly nature, whose most cherished purpose was to help those who were in distress.

We would make these sentiments a part of our permanent records and transmit copies to the members of the bereaved family.

JOHN H. NICHOLS.
HENRY R. STEDMAN.
GEORGE T. TUTTLE.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, May 17, 1923

F. K. HALLOCK, M.D., *President, in the Chair*

THE DIENCEPHALIC CENTERS CONTROLLING THE ASSOCIATED LOCOMOTOR MOVEMENTS. DR. HUGO MELLA.

This article appears in full in this issue of the ARCHIVES.

QUADRANTIC MUSCULAR CONTROL BY THE VESTIBULAR APPARATUS. A PRELIMINARY REPORT ON THE RESULT OF EXPERIMENTS ON THE VESTIBULAR APPARATUS OF THE PIGEON. DR. C. L. WOOLSEY.

Bodily movements may take place in a horizontal or a perpendicular plane, or in a resultant of both planes. Horizontal movements may be linear movements forward, backward, to the right, or to the left. Perpendicular movements may be upward or downward, in the right anterior quadrant (R. A. Q.), in the right posterior quadrant (R. P. Q.), in the left anterior quadrant (L. A. Q.), or in the left posterior quadrant (L. P. Q.), or the resultant of movements in any two contiguous quadrants. Experimental lesions of the vestibular end organ or its pathways produce certain muscular reactions, which in all probability are due to a disturbance in muscle tonus. Lesions of the vestibular end organ, or its pathways, may be stimulating or destructive. Stimulating lesions may be produced by mechanical, electromechanical, thermal, or chemical means. Mechanical stimulating lesions have been accomplished by gently inserting a horse hair or an enameled copper wire, 0.0035 inch in diameter, into a fistula in a semicircular canal and thence to the vestibular end organ.

Electrical Stimulation.—The field of operation is prepared—and the canals exposed—anesthesia is suspended until the pigeon recovers consciousness (profound anesthesia masks movements from vestibular stimulation), then a fistula into a semicircular canal is made allowing the endolymph to escape. The field of operation is thoroughly dried by alcohol, and an enameled copper wire, 0.0035 inch in diameter, is inserted until certain nystagmoid movements are noted. The wire is withdrawn slightly and the cavity filled with dental cement. By this method the wire is held in situ, and stimulation may be applied with comparative ease. Two or more canals may be stimulated simultaneously.

Thermal Stimulation.—This is produced by douching the ears with hot or cold water, or by applying heat or cold over the mastoid area.

Chemical Stimulation.—This is produced by injecting solutions directly into the endolymph channel.

Destructive Lesions.—These may be produced by a vigorous application of any of the methods used to produce stimulating lesions.

Valuable data in regard to quadrantic vestibular control may be obtained if individual ampullae are destroyed by the direct application of a red hot cautery to the bony ampulla, thereby causing an escharotic lesion of the vestibular end organ contained therein.

Experimental Data.—Linear movements, forward, backward, to the right, or to the left, are influenced by stimulating or destructive lesions of the end organ of the horizontal canals. The effects of a stimulating lesion are directly the opposite of the effects of a destructive lesion. If a horizontal canal is opened under profound etherization the escape of the endolymph rarely produces vestibular syndromes, but if etherization is suspended, and the pigeon is allowed to regain consciousness, the escape of the endolymph is accompanied by nystagmoid movements of the head and eyes. The slow pull is toward the opposite side, while the quick phase is toward the operated side. These movements cease with cessation of endolymph flow. If a horse hair or a wire is inserted into the canal and the end organ is gently stimulated, a severe tonic muscular contraction takes place, drawing the head to the opposite side in a horizontal plane. This contraction persists for from two to four seconds, and is followed by nystagmoid movements of the head and eyes; the slow pull is to the opposite side, while the quick movement is toward the operated side. If the lesion is a destructive one (destruction of the vestibular end organ), the nystagmoid movements of the head and eyes will be reversed; that is, the slow movement will be toward the operated side while the quick movement will be toward the unoperated side. The slow movement toward the operated side causes the pigeon to turn toward the operated side. Linear forward flight, at first, is impossible. If both the ampullae of both horizontal canals are destroyed a fine horizontal tremor is noted and a coarse pendulum movement of the head from side to side. The pigeon turns to either side, and flies upward in corkscrew fashion. Eighteen months after operation the above described symptoms persist.

Movements upward or downward in the right anterior quadrant, left anterior quadrant, right posterior quadrant, or the left posterior quadrant, seem to be influenced by stimulation or destruction of the ampulla of the vertical canals.

Stimulating the ampulla of the right anterior vertical canal causes a slow pull of the head into the left anterior quadrant (and vice versa). If the ampulla is destroyed the pigeon topples forward into the right anterior quadrant. Linear forward flight and upward flight are not greatly disturbed until movements are attempted in the right anterior quadrant, then the pigeon will "side slip" into the right anterior quadrant and fall.

Stimulating the ampulla of the right posterior vertical canal causes a slow pull of the head into the left posterior quadrant. If the ampulla is destroyed the pigeon topples into the right posterior quadrant, or sits on his tail. In flight he frequently turns over backward and falls into the right posterior quadrant.

If the ampulla of the left anterior vertical canal and the ampulla of the right posterior canal are destroyed, a rotary pendulum movement will be noted (the head will be rotated slightly upward—the bill toward the right), forward downward through the left anterior quadrant, into the right anterior quadrant, then upward and backward toward the right posterior quadrant. A fine vestibular rotary tremor is also noted. The pigeon topples forward into the left anterior quadrant, or falls backward into the right posterior quadrant.

If the ampullae of the right anterior vertical canal and the left posterior canal are destroyed, the movements will be the reverse of the movements in the experiment just described.

A number of patients have been examined in the Neurological Department of the Massachusetts General Hospital who have symptoms comparable to experimental quadrantic vestibular syndromes in the pigeons cited. Several cases of so-called spasmodic torticollis manifest these symptoms, and by caloric tests have shown abnormalities that would strongly point to tract lesions as a probable cause of the peculiar head movements and drawing sensations in different neck muscles.

Conclusions.—Vestibular lesions may be stimulating or destructive. The symptoms of stimulating lesions are the reverse of the symptoms of destructive lesions. Body movements in the right anterior quadrant, left anterior quadrant, right posterior quadrant and left posterior quadrant, are influenced by stimulating or destructive lesions of the vertical canals, while lesions of the horizontal canals, or their tracts, influence linear horizontal movements.

Analogous symptoms in humans would lead one to suspect lesions of the vestibular end organs, or its pathways, in a great number of the so-called habit spasms, or spasmodic torticollis, in which quadrantic vestibular symptoms are noted.

DISCUSSION

DR. PERCIVAL BAILEY: These clever experiments of Dr. Woolsey are of the utmost importance. I cannot but feel, however, that labyrinthine disturbances must be very rarely the initiating factor in torticollis. We recently had a case at the Brigham Hospital which was relieved by intraspinal section of the eleventh nerve. In this patient we were never able to see a nystagmus nor any other evidence of labyrinthine disturbance. The cases cited by Dr. Woolsey are very suggestive, and it may very well be that in certain predisposed individuals movements of the head and neck of vestibular origin might set the pattern for a habit spasm of this type.

DR. E. W. TAYLOR: From a clinical standpoint we have been much interested in Dr. Woolsey's work; although he has not absolutely proved his point, it is interesting that he has at least begun a demonstration of the relation of labyrinthine disturbance to gross muscular movements. Many of these cases of torticollis, by some regarded as psychogenic or partly psychogenic in origin, have actually never been properly explained. He seems to show that there is a connection, and in the case to which he referred there is undoubtedly a relationship between the torticollis-like movements and the disturbance in the labyrinth. As a matter of fact, it is a case which we would formerly have regarded as a beginning torticollis of the ordinary type without reference to ear involvement. This is work of the greatest practical significance as demonstrating a possible explanation of some, at least, of these hitherto mysterious cases.

DR. WOOLSEY: In regard to the origin of the quick phase of nystagmus, I believe that we do not know the mechanism of this movement. There seem to be balancing forces acting through the basal ganglions, vestibular end organs, and the cerebellum, which control muscle balance. I believe it will be impossible to explain the mechanism of the quick and slow phase of nystagmus until we know more about the lenticulovestibulocerebellar connections. In deeply anesthetized pigeons the nystagmus is produced with less frequency than in the normal pigeon, which leads one to think the cerebrum plays an important part in the solution of the quick and slow movements of nystagmus.

THE CEREBROSPINAL FLUID PRESSURE IN EXPERIMENTAL EPILEPSY. SOME PRELIMINARY OBSERVATIONS ON CEREBROSPINAL FLUID, VENOUS AND ARTERIAL PRESSURE IN EXPERIMENTAL CONVULSIONS.

Dr. Maxwell E. Macdonald.

Thujon, the convulsive agent used, is the active principle of absinthe and is generally classified pharmacologically in the camphor group. The exact point of its action is not definitely known although Hildebrant, working on the camphor group of drugs in 1902, concluded that thujon acted on the medulla primarily and the vasomotor center specifically.

It is sufficient for our purpose to say that the march of events during a convulsion produced by thujon, is very similar to that seen during an epileptic fit. Within a few seconds after the drug is given intravenously, the animal moves in a restless, uneasy manner, and there is a constriction of the pupils and the peripheral vasomotor system. There follow immediately retraction of the head with tonic extensor spasms of the forelimbs and more rarely of the hind limbs. These are followed by clonic spasms, dilatation of pupils, exophthalmos, unconsciousness, and loss of control of sphincters. Under anesthesia it is necessary to give a larger dosage, but the course of events is similar.

In the following experiments ether was given by the tracheal route.

Experiment 1.—Cat. Venous pressure apparatus was attached to the jugular vein and a trephine opening was made in the temporoparietal region; the dura was incised, and the hole closed by sealing a funnel-shaped glass attached to a membrane manometer over it. This made a closed system so that any change in the air volume would be registered on a kymograph. Twenty mils of 20 per cent. thujon in cod liver oil was given intravenously. The first chart (charts demonstrated) shows the marked oscillations of the venous pressure during the convulsion: from 5 cm. to 16 cm. in one convulsion and from 4 cm. to 23 cm. in another. The kymograph record shows clearly the fact that there was a retraction and bulging of the brain.

Direct observations were also made through the trephine opening. Just before the convulsion the brain appeared to shrink and blanch and at this moment the fluid (Ringer's) in a manometer connected with the lateral ventricle, fell to a low point. After the momentary blanching and shrinking, the brain surface became congested and swollen, pushing through the trephine opening. At the same moment the fluid in the manometer rose to a high point.

Experiment 2.—Cat. In this animal instead of a large opening, one just sufficient to admit a needle was made. A manometer was connected directly with the ventricle. The tracings show a distinct drop in cerebrospinal fluid pressure before the convulsion and a subsequent rise in venous and cerebrospinal fluid during the convulsion. One part of the chart shows a gradual fall in cerebrospinal fluid pressure while the animal was breathing rapidly. This has been observed several times and leads one to think that the respirations in themselves are not the cause of the rise in pressure.

Experiment 3.—Puppy. Similar changes in pressure were revealed, namely, a drop before and a rise during the convulsion. Direct observation on this animal showed the initial blanching before and the protrusion with congestion, during the convulsion.

Other charts showed a similar sequence of events with manometer records of cistern pressure.

A kymograph record of the arterial pressure during a thujon convulsion shows that there is a slight rise at the end of the injection. This is very transitory; the pressure gradually drops and stays lower than normal during the convulsion. Following, there is a gradual return to normal level.

Three interesting clinical observations have been made recently during lumbar puncture on epileptics. A sudden drop occurred while the readings were being taken. Immediately after, the pressure rose as the convulsion occurred.

Pollock has made tracings of the blood pressure during a petit mal attack which show a preliminary rise in blood pressure at twenty-six to sixty seconds, and a sudden marked drop at nine to twelve seconds before the convulsion. The blood pressure remained low during the attack. The observations of Foster Kennedy and John Hartwell of the brain of a patient during an epileptic fit showed as the initial sign a sudden whitening of the cortex which was immediately replaced by an extreme venous engorgement with the protrusion of the brain beyond the level of the operative bone defect.

It is interesting to note the fact that in quite a number of epileptics the ventricles have been found dilated. We have produced a slight dilatation of the ventricles in young rabbits by giving them a large number of convulsions over an extended time. It is therefore possible that the enlarged ventricles in human cases are a result of the repeated convulsions.

The results of these preliminary observations in thujon convulsions seem to show that there is an initial drop in cerebrospinal fluid pressure coincident with the blanching and retraction of the cortex and a subsequent rise during the stage of congestion; that the venous pressure follows the cerebrospinal fluid pressure; that the marked oscillations in pressure are not due, entirely at least, to the respirations; that (at least in one case) there is a lowering of arterial pressure.

There is some association between these experimental and several clinical observations. The results of the work are by no means conclusive, and are presented only as they point to paths of aproach to the problem.

DISCUSSION

Dr. Hugo Mella: I do not wish to strike a discordant note, but I did not find a rise in pressure in the case alluded to by Dr. Macdonald, unless he refers to the rise back to normal after the convulsion. In doing a lumbar puncture on a young man who gave a history of convulsions over a period of two years after discharge from service, while waiting to get a normal reading before removing any fluid the pressure suddenly dropped and the column of fluid disappeared from the manometer. The patient commenced to move and went through a typical convulsion. I kept my hand on the needle until he came out of the attack and after the convulsion was over, the pressure came back to its original point of about 150. Throughout the attack the lumbar puncture apparatus was perfectly connected.

I think the experimental results of Dr. Macdonald have been quite contrary to this observation. This patient showed typical hysterical attacks of an emotional sort, and the question arises, was it possibly a functional attack, and is there a difference in the cerebrospinal fluid pressure in the functional and in the idiopathic attack?. Might it be something of that sort?

Dr. Percival Bailey: It would be interesting in these animals to follow the intracranial venous tension, since Becht has shown that the cerebrospinal

fluid pressure follows closely the venous pressure. I have seen patients, during operation on the brain under local anesthesia, go into convulsive attacks without observing any change in the caliber of the cerebral blood vessels exposed.

DR. DONALD GREGG: I have seen conjunctival hemorrhage after attacks of severe epileptic convulsions. Has that occurred in the experimental cases?

DR. MACDONALD: I have never seen conjunctival hemorrhages. In one case after repeated severe convulsions, toward the end of his wild clonic episode, the animal broke his back with a resultant lower paraplegia. Two days later at necropsy a fracture was found at the seventh dorsal vertebra. Besides local injury, many small hemorrhages were found in the mucous membranes of the stomach, intestine and bladder. Whether these were the result of the convulsion *per se* or whether they followed the injury I do not know, but the latter is more probable.

STUDIES IN THE CHEMISTRY OF THE BLOOD IN EPILEPSY.

DR. WILLIAM G. LENNOX (by invitation).

The following constituents of the blood, viz., non-protein nitrogen, urea nitrogen, amino-acid nitrogen, uric acid, creatinin, sugar, and alkali reserve have been determined in a group of more than 100 epileptic patients. Practically all determinations were within the limits of normal. The values bore no relationship to the time or frequency of convulsions. Similar determinations were made on the blood of seven epileptic patients during and following prolonged starvation. Starvation was absolute, except for water, and continued for from eleven to twenty-one days. All these patients showed remarkable increase of the blood uric acid (from a pre-starvation level of 3 to 5 mg., to a starvation peak of 8 to 16 mg. per 100 c.c. of blood). This increase was found to be due to a failure of the kidneys to eliminate uric acid. It occurred in a normal individual who underwent a short fast. In one of the patients, at the end of starvation, the non-protein and urea nitrogen rose respectively to the remarkably high concentration of 300 and 240 mg. per 100 c.c. of blood. It is believed that these great fluctuations in the non-protein nitrogenous constituents of the blood during fasting have nothing to do with the fact that the patients were epileptic. During starvation convulsions were decreased; therefore, the observations furnish additional evidence that in epilepsy convulsions are not initiated by increase of uric acid, non-protein nitrogen, or urea nitrogen in the blood.

DISCUSSION

DR. STANLEY COBB: Dr. Lennox' work is in the stage of experimentation; the main point of interest now, I think, is that we seem to be able in some cases to stop the attacks by a starvation period. We therefore want to know what happens in starvation to the body metabolism. We are searching along these lines and may eventually reach a possible explanation. One point of interest, as you probably noticed on the charts demonstrated, was the extremely high uric acid. What that means we do not as yet know.

ELECTROMYOGRAPHIC STUDIES OF MUSCULAR FATIGUE IN MAN.

DR. STANLEY COBB and DR. ALEXANDER FORBES.

In neurology and general medicine not enough attention is given to muscle. Although this tissue comprises a major part of our body weight we rarely take into account its great metabolism, nor consider its activity and fatigue.

The study of nerve and muscle relationships is still a great field for research. But the study of muscular fatigue is so complicated by psychologic factors, that a method of accurately recording any of its concomitant phenomena may be of value. The present study was undertaken because it applies a new combination of methods to the study of fatigue in the hope of elucidating to some extent the complex problem.

Muscular fatigue of the flexors of the wrist (principally the flexor carpi radialis) was studied in ten different individuals. In the first eight experiments the isotonic contraction was used. This was accomplished by constructing a large ergograph to which the right arm was strapped. The hand was inserted into a heavy woolen glove thickly coated with plaster of Paris, so that the finger and metacarpal joints were immovable. This so fixed the limb that motion was possible only at the wrists. A wire was attached to the plaster glove, and this ran over a pulley to the weight which hung below. The action-currents of the contracting muscle were led off by placing non-polarizable electrodes on the arm; these electrodes were connected with the galvanometer, completing a circuit, and the oscillations were recorded on a rapidly moving film. Besides recording the movements of the galvanometer string on the moving film a lever was so arranged that it cast a shadow on the film, simultaneously recording the mechanical movement of the wrist in lifting the weight. Thus the records of the mechanograms and electromyograms are synchronous and indicate simultaneous mechanical and electrical phenomena. In the last ten experiments isometric muscular contractions were studied The arm was fixed as before, but the hand was also strapped down firmly, and the subject was told to "pull as hard and steadily as possible" against the immovable strap.

Using the method above described eighteen experiments were performed on ten different individuals. The data obtained are summarized in the accompanying table.

TABLE—*Electromyographic Changes with Fatigue*

Experiment	Subject	Time in Seconds Taken to Cause Fatigue	Change in Frequency of Action-Currents, per Sec.	Change in Amplitude of Main Waves, per Cent.	Total Amount of Work in Cm. Kg.	Change in Resistance in Ohms	
1	T.	150	— 7	+127	688	.....	Isotonic
2	S. C.	90	— 4	+ 70	1,005	.....	Isotonic
3	S. C.	190	—10	+ 51	1,458	10,000 to 10,000	Isotonic
4	A. F.	390	— 1.5	— 0	4,080	17,000 to 18,000	Isotonic
5	O.	255	—14	+ 80	2,760	.....	Isotonic
6	B.	405	—10	+100	4,387	45,000 to 30,000	Isotonic
7	S. W.	330	—18	+ 67	1,431	11,000 to 10,000	Isotonic
8	O. R. F.	300	—10	+183	3,300	11,000 to 10,000	Isotonic
Average		264	— 9	+ 85			Isotonic
9A	S. C.	95	—24	+ 43	.....	.....	Isometric
9B	S. C.	60	—20	+ 24	.....	.....	Isometric
10	S. E. H.	120	— 7	+150	.....	.....	Isometric
11	S. C.	60	—26	+116	.....	.....	Isometric
12	H. W. S.	75	—18	+100	.....	.....	Isometric
13	H. B. C.	75	—24	+ 80	.....	.....	Isometric
14	S. C.	70	—10	+ 75	.....	.....	Isometric
15	S. C.	65	—24	+111	.....	.....	Isometric
16	S. C.	80	—21	+ 29	.....	110,000 to 114,000	Isometric
17	S. E. H.	50	—18	+ 56	.....	96,000 to 103,000	Isometric
18	A. F.	75	—23	+ 25	.....	40,000 to 48,000	Isometric
Average		75	—20	+ 73			Isometric

In looking over the data presented in the table, it is seen that two changes in the electromyogram usually appear with fatigue. In the first place the frequency (rate per second) of the action-currents is decreased. Secondly, there is usually a distinct increase in the amplitude of the waves, indicating that action-currents of greater voltage are produced in the fatigued muscle. This decrease in frequency and simultaneous increase in size of action-currents, which we have observed in fatigue, may be explained theoretically either by assuming a resistance or partial block to develop at the neuromuscular junction, or by assuming that fatigue reduces the excitability of the muscle fibers without causing a corresponding reduction of the size of response of which they are capable. Finally, these observed effects might be explained as the result of an increased frequency of discharge of nerve impulses from the motor centers, but since there is no positive evidence in favor of this latter view and much evidence tending to localize the effects in the muscle, this explanation may probably be discarded in favor of one of the other two.

DISCUSSION

DR. PERCIVAL BAILEY: It would be interesting to know whether the excitability of a muscle decreases in fatigue states. It is generally accepted that the chronaxie of an excitable tissue varies only with the temperature, but I know of no observations on the fatigue state.